

From the Department of Clinical Neuroscience, Division of Forensic Psychiatry

# **“Dr Jekyll and Mr Hyde?”**

**Abuse of potent benzodiazepines, exemplified by  
flunitrazepam, in mentally disordered male offenders**

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## Abstract

Flunitrazepam (FZ) is an example of a sedative-hypnotic benzodiazepine whose pharmacokinetic properties include a rapid onset of action and an intermediate duration of action. It has a high affinity to central benzodiazepine receptors and affects them profoundly. These properties, and its profile of activity, increase the probability of abuse by those who have access to it. Known side effects of FZ are abuse and amnesia. FZ is widely abused and it has become a drug of choice among opioid abusers, as a club drug, and as a classic “date-rape” drug. FZ is often involved in fatal intoxication. It is therefore expected that FZ abuse is common in serious offenders. I have studied the reasons for FZ abuse and mapped the prevalence of the abuse, with the objective of studying the personalities and the background factors of the abusers, and of drawing some conclusions about assessment procedures of FZ abuse and the position of FZ in society.

The participants in the studies summarised here were fifty-six juvenile delinquents from Swedish youth correctional institutions, aged 14-20 years, and sixty non-psychotic male offenders referred for a forensic psychiatric evaluation (FPE), aged 16-35 years. The participants answered questions regarding their abuse, and this enabled us to understand why they abused just FZ (and not another substance). The participants also completed a number of self-reported inventories, which enabled us to obtain measures of personality traits. They were also rated for psychopathy. Five forensic psychiatric cases of FZ abusers were studied in more detail. Furthermore, the forensic psychiatric participants’ psychiatric diagnoses, and both groups’ crime-related measures, were obtained from their files.

About 40% of the juvenile delinquents and 30% of the offenders referred for a forensic psychiatric evaluation abused FZ. The main reason for the FZ abuse was to change a perception of reality and to obtain an increased feeling of power and self-esteem, a feeling that everything was possible. Both samples of offenders differed from the normal population in many personality traits, suggesting that the participants possessed a high level of vulnerability for developing mental disorders, but only a few differences in personality traits were found between FZ abusers and non-FZ abusers. The juvenile delinquent FZ abusers had higher scores than non-FZ abusers in the verbal aggression and sensation-seeking boredom susceptibility scales. In the juvenile sample, FZ abuse was associated with the abuse of amphetamines and/or cocaine, cannabis, and opiates, and with childhood psychological/psychiatric contact, with living in a metropolitan housing area, and with recidivism into crimes leading to care in a juvenile correctional institution. In this sample, FZ abuse was also associated with weapons offences and narcotics-related crimes. In the forensic psychiatric sample, FZ abuse was significantly associated with previous admission to an FPE, and convictions for robbery, for weapons-related offences, for narcotics-related offences and for theft. The results show that FZ is more common in offenders who score high on Facet 4 (Antisocial) in the Hare psychopathy model, and that FZ abuse has high correlation with Item 20 (Criminal versatility). All of the FZ abusers reported side effects from FZ that resulted in the brutality of their violent acts and anterograde amnesia. FZ abusers, when intoxicated with FZ, had a reduced capacity for both empathy and anticipatory anxiety, in contrast to their “daily” behaviour and “ordinary” (i.e., without the influence of the FZ) personality characteristics. They were not characterised by classic characteristics of psychopathy, such as lack of empathy. This may indicate that FZ induces psychopathic-like state-dependant (FZ intoxication) traits, and temporary dissociate states (“Dr Jekyll and Mr Hyde?”).

In conclusion, FZ abuse is common in the population of young offenders with mental disorders, and FZ is often used for nonmedical purposes. The practical implications of these conclusions are that clinicians and those who develop or manage therapeutic programs should be aware of FZ abuse when choosing the most effective treatment for male offenders. General practitioners who prescribe potent sedative compounds should be aware of their possible adverse effects. The availability of FZ should be limited further, because FZ is frequently abused in vulnerable male offenders, and because FZ has serious adverse mental health-related effects and is related to robbery and weapons-related crimes.

*Key words:* Flunitrazepam (FZ) abuse, side effects of FZ, offenders referred to forensic psychiatric evaluation, juvenile delinquents, personality traits, psychopathic traits and lifestyle (PCL-R).

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To Robert

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“Everything is possible”

## List of original studies

This thesis is based on the following studies, which will be referred to in the text by Roman numerals (Studies I-IV and the Letter to the Editor have been reprinted with the kind permission of the publishers):

- I. Dåderman, A. M., & Lidberg, L. (1999). Flunitrazepam (Rohypnol) abuse in combination with alcohol causes premeditated, grievous violence in male juvenile offenders. *Journal of the American Academy of Psychiatry and the Law*, 27, 83-99.
- II. Dåderman, A. M., & Edman, G. (2001). Flunitrazepam abuse and personality characteristics in male forensic psychiatric patients. *Psychiatry Research*, 103, 27-42.
- III. Dåderman, A. M., Fredriksson, B., Kristiansson, M., Nilsson, L.-H., Lidberg, L. (2002). Violent behavior, impulsive decision-making, and anterograde amnesia while intoxicated with flunitrazepam and alcohol or other drugs: A case study in forensic psychiatric patients. *Journal of the American Academy of Psychiatry and the Law*, 30, 238-251.
- IV. Dåderman, A. M., Edman, G., Wirsén Meurling, A., Levander, S., & Kristiansson, M. (2005). *Psychopathic traits and lifestyle in flunitrazepam abusers*. (Submitted for publication).

The following Letter to the Editor regarding erroneous information in Study III is also included:

Dåderman, A. M., Fredriksson, B., Nilsson, L.-H., Kristiansson, M., & Lidberg, L. (2004). The abuse of a sleeping pill that contains the active substance flunitrazepam (FZ) – for example, Rohypnol – and the effects of FZ intoxication, such as enhanced violence and disturbed memory. *Journal of the American Academy of Psychiatry and the Law*, 32, 467-468.

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## **ABBREVIATIONS**

ANOVA	one-way analysis of variance
BS	boredom-susceptibility (a sub-scale from the SSS-V)
CNS	central nervous system
CSF	cerebrospinal fluid
Dis	disinhibition (a sub-scale from the SSS-V)
DSM-IV	diagnostic and statistical manual of mental disorders, of the American Psychiatric Association (the 'IV' is the version number)
EPQ	Eysenck Personality Questionnaire
EPQ-I	Eysenck Personality Questionnaire together with the Impulsiveness scale from the IVE
ES	experience-seeking (a sub-scale from the SSS-V)
FPE	forensic psychiatric evaluation
FZ	flunitrazepam
GABA	gamma-aminobutyric acid
GAF	Global Assessment of Functioning scale
5-HIAA	5-hydroxyindoleacetic acid
5-HT	5-hydroxytryptamine (serotonin)
IVE	Impulsiveness-Venturesomeness-Empathy inventory
KSP	Karolinska Scales of Personality
MAO	monoamine oxidase
MNT	Marke-Nyman Temperament inventory
PCL-R	Psychopathy Checklist-Revised
SSS-V	Zuckerman Sensation-Seeking Scales (the 'V' is the version number)
SRB	Swedish standard intelligence battery
TAS	thrill- and adventure-seeking (a sub-scale from the SSS-V)
WAIS-R	Wechsler Adult Intelligence Scale-Revised
WHO	World Health Organisation

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## INTRODUCTION

### *Benzodiazepines*

Benzodiazepines are psychotropic drugs – drugs that affect the mind and alter the mood (Carlsson, 1979; Cohen, 1987; Kenyon, 2005; Priest, Vianna Filho, Amrein, & Skreta, 1980; Roos, 1979; Söderpalm, 1987; World Health Organization, 1996). Benzodiazepines were discovered in the early 1960s (the first benzodiazepine, chlordiazepoxide, was introduced in 1958), and are an effective family of anxiolytics (from “anxiety” and the Greek *lyein*, “to loosen or dissolve”).

Table 1 shows the benzodiazepines that are currently (18 October 2005) available in Sweden, and their pharmacokinetic properties (World Health Organization, 1996). For comparative purposes, three “newer” benzodiazepine-like compounds are also presented, along with their pharmacokinetic properties (for references see Table 1).

All benzodiazepines are classified as narcotic substances in Sweden; FZ is classified as a Schedule II substance (the same schedule as morphine), while the remaining benzodiazepines are classified as Schedule IV substances (the same schedule as Subutex). (For information concerning these schedules see World Health Organization, 2003, p. 3.) Zolpidemtartrat is classified in Sweden as a Schedule IV substance and zopiklon as a Schedule V substance. Information about the classification of the newest compound, zaleplon, is not available (“narkotikaklassade humanläkemedel”, 2005).

Table 1

*Benzodiazepines currently (18 October 2005) approved for sale in Sweden by The Swedish Medical Products Agency: their generic names as they are presented in the Swedish pharmacy compendium FASS and the manufacturers (“sök läkemedel”, 2005), and their basic pharmacokinetic properties (World Health Organization, 1996). Three newer benzodiazepine-like compounds are also presented*

Generic name	Product name	Absorption time (h) <sup>1</sup>	Elimination half-life (h) <sup>2</sup>	Manufactured by
<i>Benzodiazepines</i>				
Alprazolam	Alprazolam	1-2	10-12	STADA Arzneimittel
	Alprazolam, STADA			STADA pharm
	Alprazolam Merc NM			Merc NM
	Xanor Depot			Pfizer
	Xanor			Pfizer
Diazepam	Diazepam Desitin	0.5-1.5	15-60	Desitin
	Diazepam novum <sup>3</sup>			Alpharma
	Stesolid prefill			Alpharma
	Stesolid <sup>3</sup>			Alpharma
Flunitrazepam	Flunitrazepam Merck NM	1-1.5	20-30	Merck NM
	Fluscand			Teva
Klonazepam	Iktorivil <sup>3</sup>	3-14	18-50	Roche

Lorazepam		1-2	10-12	
	Temesta			Wyeth
Midazolamhydroklorid		0.25	1.5-3	
	Dormicum <sup>3</sup>			Roche
	Midazolam Alparma			Alparma
	Midazolam Fresehins Kabi			Pharmathen
	Midazolam Hameln			Epipharm
	Midazolam Mayne			Mayne Pharma
Nitrazepam		1.5-2	18-25	
	Apodorm			Alparma
	Mogadon			MediLink
	Nitrazepam Recip			Recip
Oxazepam		1-2	8-10	
	Oxascand			Teva
	Sobril			Pfizer
Triazolam		0.5-1	3-4	
	Halcion			Pfizer
	Triazolam Merc NM			Merc NM
<i>“New” benzodiazepine-like non-benzodiazepine sedatives/hypnotics</i>				
Zaleplon		≤1.0 <sup>4</sup>	1.0 <sup>4</sup>	
	Sonata			Wyeth
	Zarene			Wyeth
Zolpidemtartrat		0.5 <sup>4</sup>	2.5 <sup>4</sup>	
	Eanox			Desitin
	Stilnoct			Sanofi-Synthelabo
	Stilnoct			Orifarm
	Stilnoct			Paranova
	Stillnox			Medartuum
	Zolpidem Generics			Generics (UK)
	Zolpidem Genthon			Genthon
	Zolpidem Merc NM			NM Pharma
	Zolpidem Stada			STADA Arzneimittel
Zopiklon		“rapid” <sup>5</sup>	3.5-6.5 <sup>5</sup>	
	Imovane			Meda
	Zopiclone Alparma			Alparma
	Zopiklon Merc NM			Merc NM

*Notes:* <sup>1</sup>The time required for “the onset of action, that is: the time period between drug ingestion and the point at which the clinical action occurs” (World Health Organization, 1996, p. 7). The values are based on information presented by World Health Organization (1996, Table 1). <sup>2</sup>The time required reaching a steady-state concentration. According to World Health Organization (1996) “it is generally accepted that a period of time equivalent to five times the half-life of the drug (and active metabolites) is necessary to reach a steady-state concentration” (p. 24). The values are based on information presented by World Health Organization (1996, Table 1). <sup>3</sup>Also available as an injection form. <sup>4</sup>See Moore (2000, Table 1). <sup>5</sup>According to Fernandez, Martin, Gimenez, and Farinotti (1995)

Table 1 shows that benzodiazepines differ in their *pharmacokinetic* properties, such as the rate of onset of action, and the duration of action. The information is valid for normal administration forms, and it should be kept in mind that benzodiazepine abusers may use other forms, such as inhalation or injection (see below). It is known that substance abusers wish to achieve the desired effect as rapidly as possible.

The inspection of Table 1 suggests that FZ is a benzodiazepine with a rapid<sup>1</sup> onset of action and intermediate duration of action. This profile of activity make FZ one of the most potent benzodiazepines, and it increases the probability of its abuse by those who have access to it.

*Flunitrazepam – a drug of choice among subjects from various populations*

This thesis focuses on FZ abuse, because FZ is the only benzodiazepine that is used among other substances (such as GHB) as a club drug (see e.g., Gahlinger, 2004; Smith, Larive, & Romanelli, 2002); it has become a benzodiazepine of choice among opioid abusers (Navaratnam & Foong, 1990; Woods & Winger, 1997); it shows greater abuse liability than triazolam (Mintzer & Griffiths, 1998); it is a classic “date-rape” drug (Anglin, Spears, & Hutson, 1997; Schwartz, Milteer, & Lebeau, 2000); it is involved in many fatal intoxications (Carlsten, Waern, Holmgren, & Allebeck, 2003; Druid & Holmgren, 1997; Druid, Holmgren, & Ahlner, 2001); it is the only benzodiazepine used by street children (Inciardi & Surratt, 1998; Salem & El-Latif, 2002); it is frequently abused among young Swedish offenders (Studies I and II); it is the drug that constitutes most of the illegally imported benzodiazepine that enters Sweden – 90% of all tablets illegally imported (i.e., tablets of substances classified as narcotic substances<sup>2</sup>) into Sweden, were Rohypnol tablets (746,907 Rohypnol tablets were seized in Sweden in 2002, according to Jonas Karlsson, Tullverket Mälardalsregionen, unpublished report, 2003); the *abuse* of FZ is the most frequent mental health-related adverse effect of its use according to spontaneous reports from general practitioners in 70 countries, including Sweden, (which is in contrast to, for example diazepam, where other mental health-related adverse effects than abuse are the most frequently reported: see Figures 3 and 4); and it is the only benzodiazepine that has been moved from Schedule IV (controlled substances) to Schedule III in an attempt by the United States Drug Enforcement Administration (DEA)<sup>3</sup> to improve its documentation (see World Health Organization, 1996, p. 3).

Description of actions taken against FZ in some countries, for example, introducing re-classification of FZ or using different measures in order to limit its availability, as well as the grounds for these decisions, is presented in Holmberg et al. (2002, Chapter 10). The World Health Organization (2001) reported that the South African Medicines Control Council has, as some other countries, withdrawn registration of all 2 mg formulation tablets and scheduled 1 mg tablets in Schedule 6 (narcotic drugs), and also decided, that “all compounds that include FZ must be reformulated to include a bitter taste and colorant in order to minimize risk of illegal use in facilitating crimes” (p. 13).

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<sup>1</sup> According to World Health Organization (1996) “those benzodiazepines which are rapidly absorbed from the gastrointestinal tract have a prompt clinical action, whereas those which are slowly absorbed have a much slower onset of action. After oral administration, the absorption of diazepam, alprazolam, desmethyldiazepam (e.g. formed from its precursor cloradiazepate), flurazepam (leading to its aldehyde and hydroxyethyl metabolites) midazolam and triazolam is very rapid. The peak plasma concentration occurs about one hour after ingestion. Such rapid absorption accounts for the acute subjective high drowsiness, ‘space-out’ feeling and/or motor impairment after the drug is ingested” (p. 7).

<sup>2</sup> There were 87 compounds (including one compound, which is used in animals only) that were classified as narcotic substances in Sweden in 2005 (“narkotikaklassade humanläkemedel”, 2005).

<sup>3</sup> The DEA is equivalent to the Swedish Medical Products Agency (Läkemedelsverket).

## Thesis delimitation and its overview

This thesis has a mainly biological orientation, and it uses a biologically oriented trait-based approach. I expect for this reason that the findings can be understood within a psychopharmacological approach. Other perspectives (such as sociological perspectives and psychodynamic perspectives) that attempt to explain criminal and addictive behaviour as a result of a glaring societal injustice, a “bad mother”, or an unsolved conflict during childhood are not presented or discussed. The biological orientation is motivated because FZ acts rapidly at the brain (for a review see DEA, 1996 and Woods and Winger, 1997), profoundly affects the benzodiazepine receptors (see the subsection *Neuropsychopharmacological properties of FZ*), and, as is expected, changes behaviour. Therefore, certain personality traits as well as psychopathic traits and psychopathic style have been studied, because they have their theoretical and empirical foundation, at least to some extent, in biological psychiatry and biological psychology (e.g., Engström, Westrin, Ekman, & Träskman-Bendz, 1999; Gustavsson, Träskman-Bendz, Higley, & Westrin, 2003; Laakso et al., 2000; Melke et al., 2001; Orelund, Hallman, & Damberg (2004); Raine et al., 2004; Söderström, Blennow, Sjödin, & Forsman, 2003; Stålenheim, Eriksson, von Knorring, & Wide, 1998; Tuvblad, Eley, & Lichtenstein, 2005). It is, however, obvious that findings from studies based on a biologically oriented approach should be discussed in the social and political context of the participants studied, because nobody acts in an empty environment.

The thesis *Introduction* consists of several subsections. The first section briefly describes legislation regarding FZ compounds in Sweden and points out that FZ is still available in Sweden. The second section describes spontaneous reports from general practitioners regarding adverse side effects of FZ. It is evident that FZ is associated with adverse side effects related to mental health, as are other benzodiazepines such as diazepam. Limitations of this thesis regarding the term “FZ abuse” are also specified in the *Introduction*. The prevalence of the abuse of FZ is presented, because one of the aims of this thesis was to establish the frequency of the abuse of FZ in the population of male offenders studied. The next section describes some known specific clinical effects of FZ on psychological functions and states in normal persons. The relationship between intoxication with FZ and violent acts is the focus of the next section. Current knowledge regarding this issue is limited to a few case descriptions. Basic concepts in neuropsychopharmacology are presented, and the neuropsychopharmacological properties of FZ are described, because FZ is an example of short-acting benzodiazepine with intermediate duration, and it is necessary to have these properties in mind when analyzing and discussing the results from the studies described in the present thesis, and because of the biological approach of this thesis. A biological “vulnerability model” is also presented. The next two sections are devoted to short explanations of the theoretical basis of the personality inventories used in the work presented in the thesis, and these sections present evidence of the predictive and discriminant validity of these inventories. This overview is presented because many researchers have suggested that people who develop any kind of addiction have a particular personality profile. This is naturally presented in detail, because personality traits are a major focus of the work described in the present thesis. Psychopathy,

according to Cleckley's concept and as measured by the PCL-R, is examined in the thesis, and the following section for this reason briefly describes the concept of psychopathy. This section also presents the aims of the work described and it lists the specific questions addressed.

The methodological issues of study design, information about the selection of samples, inclusion and exclusion criteria, ethics, procedures, the instruments used (including validity and reliability issues), data processing (including the method used in the coding and analysis process, an inductive qualitative analysis known as "grounded theory"), and statistical methods are discussed in *Methods*.

A brief presentation of the most important results of the four empirical studies, which in some cases have been revised following the original publication, corrected and accompanied by some comments and some additional analyses, is given in *Main Findings and Comments*.

Finally, *General Discussion* consists of several subsections. The first section briefly summarizes the aims and the main findings and conclusions. The next section presents general remarks concerning the work included in the present thesis, and it specifically compares the findings with other published studies. Some weaknesses in the study design and procedures are described and discussed in a subsection titled *Thesis Limitations*. The next section presents some clinical issues, possible implications for "crime scene investigations" and similar investigations regarding offenders who may have been intoxicated with FZ or other potent benzodiazepines (or benzodiazepine-like compounds), possible theoretical issues, including neuropsychopharmacological issues, and legal implications of the work presented here, and it suggests future studies. Conclusions are given at the end of the section.

## **Flunitrazepam compounds in Sweden**

FZ has been an internationally regulated substance (Schedule III) since 1983, and it has been classified as a narcotic substance in Sweden (Schedule II) since 1 May 2001. This means that all non-medical use (use without contact with the health-care system or without any confirmed chronic disease) of this compound is regarded as abuse. It is well-known among clinicians, social workers and police that FZ abusers chew the drug (in the case of Rohypnol, which has been dyed blue since 1998 "to prevent misuse" (see World Health Organization, 1998, p. 241), chewing the drug is known among FZ abusers as "eating bilberry"), swallow it, take it as a snuff (after it has been divided into pieces), smoke it, and inject it. The different forms of administration change the drug's pharmacokinetic properties and some forms make the drug very potent.

Two compounds of FZ are currently available on the legal market in Sweden (2005) in 0.5 and 1 mg tablets: Flunitrazepam Merck NM, manufactured by Merck NM, Stockholm; and Fluscand, manufactured by Teva Sweden ("sök läkemedel", 2005; see also Table 1); both compounds are white tablets. Two additional compounds were available in Sweden during the period of data collection for the studies included in the thesis: Flupam, manufactured by Tika Läkemedel, Lund; and Rohypnol, manufactured by F. Hoffman-La Roche. Flupam was withdrawn from the Swedish market in October 1998, and Rohypnol was withdrawn in January 2004. The Swedish Medical Products Agency (Läkemedelsverket) decides which drugs can be introduced

onto the Swedish market, and handles applications from manufacturers regarding the approval and withdrawal of specific compounds from the Swedish market. For example, Valium was withdrawn from the Swedish market in this way, because, according to the manufacture (F. Hoffman-La Roche), it returned to little profit. Also Rohypnol was withdrawn from Sweden for the same reason: the sale values have declined drastically (see Alvan & Eklund, 2001; Johansson, 2004). Legal issues regarding FZ in some countries, including Sweden, are outlined briefly in Study III, pp. 242-243 and in Holmberg et al. (2002, Chapter 10).

### Spontaneous reports from general practitioners regarding adverse side effects of FZ

A total of 68 spontaneous reports have been filed by general practitioners in Sweden regarding adverse side effects of FZ in the Swedish Medical Products Agency’s (Läkemedelsverket) database (Bengt Lindeskog, Läkemedelsverket, personal communication, 1 July 2005).

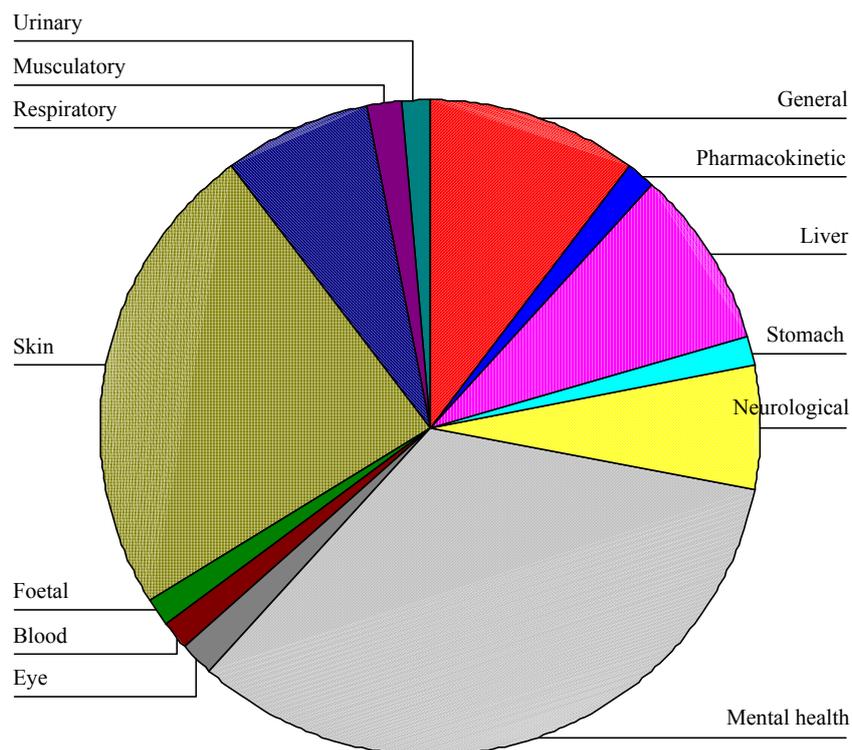


Figure 1. Proportion of adverse effects of flunitrazepam in the Swedish side effects database. The first report was recorded in 1981 and the most recent in 2004.

The association between these adverse effects and FZ has been judged by the Agency as “possible” for these 68 reports. Most of them are classified as mental

health-related side effects (Figure 1). For comparative purposes, the adverse side effects of diazepam in the Swedish Medical Products Agency's database (Bengt Lindeskog, Läkemedelsverket, personal communication, 5 July 2005) are presented in Figure 2.

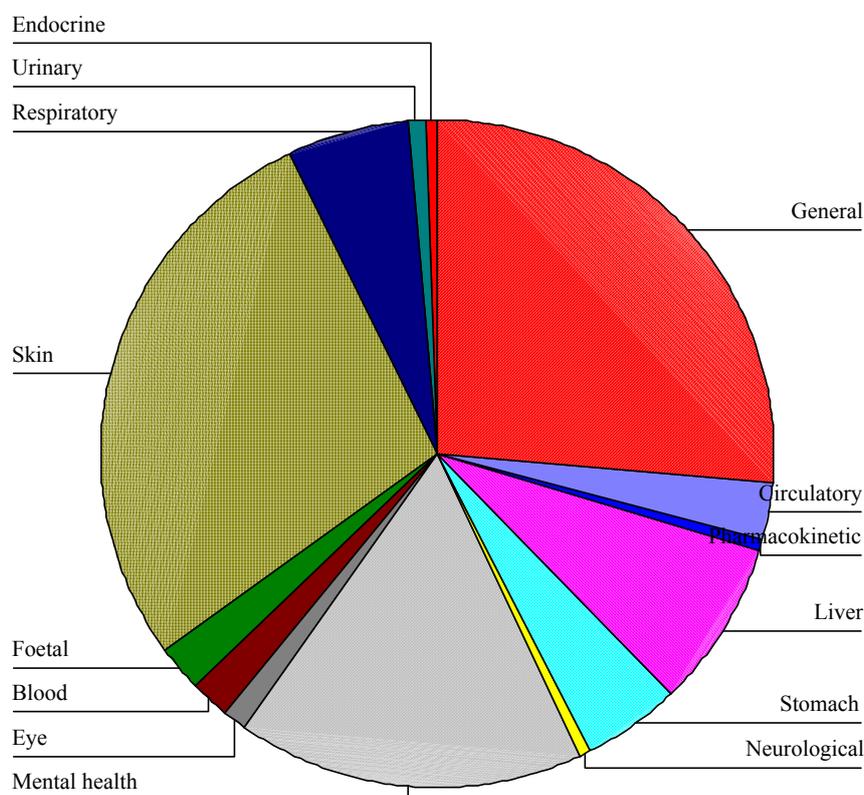
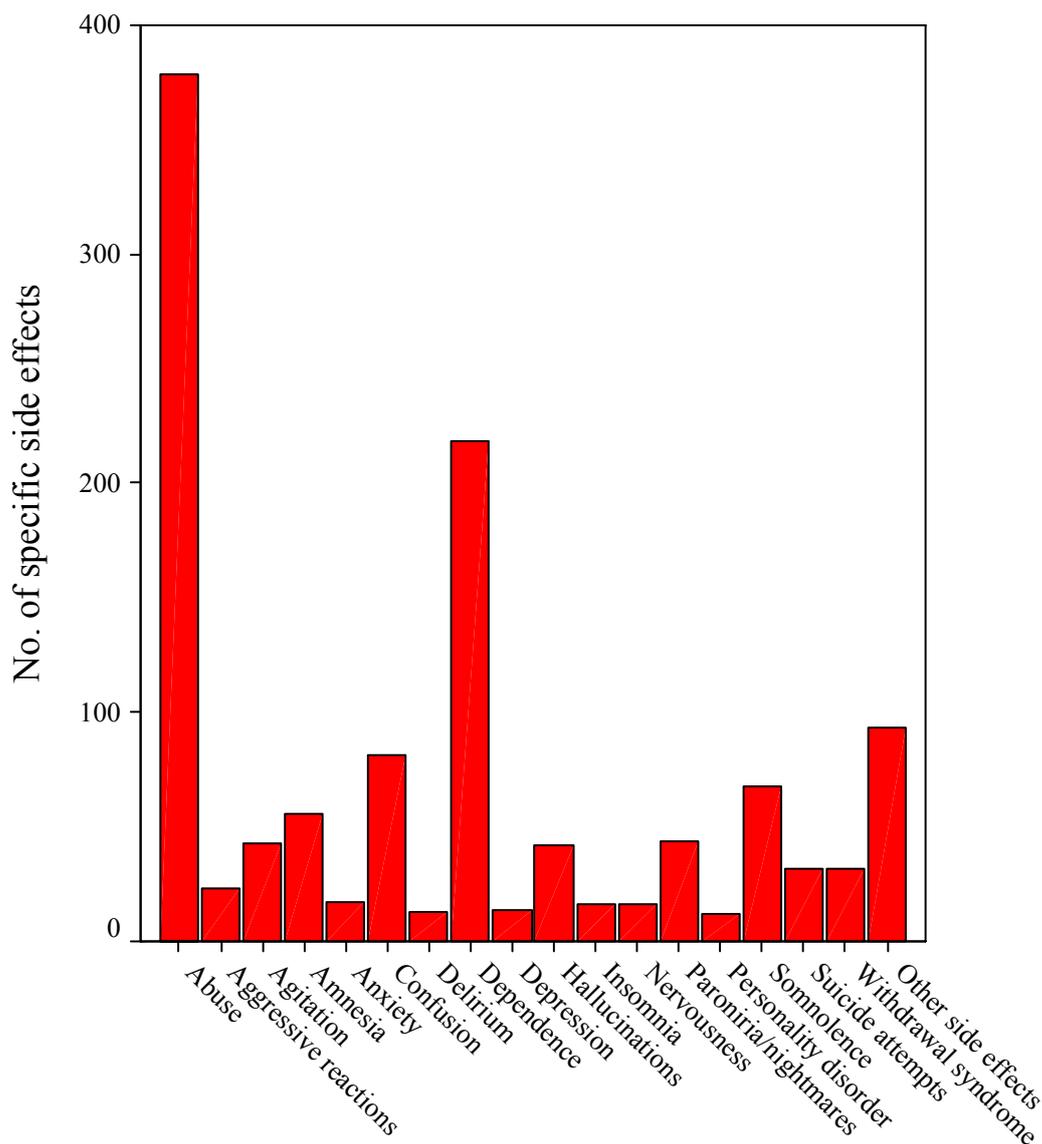


Figure 2. Proportion of adverse effects of diazepam in the Swedish side effects database. The first report was recorded in 1966 and the most recent in 2004.

Figures 1 and 2 show that the proportion of mental health-related side effects for FZ is approximately twice as large as that for diazepam.

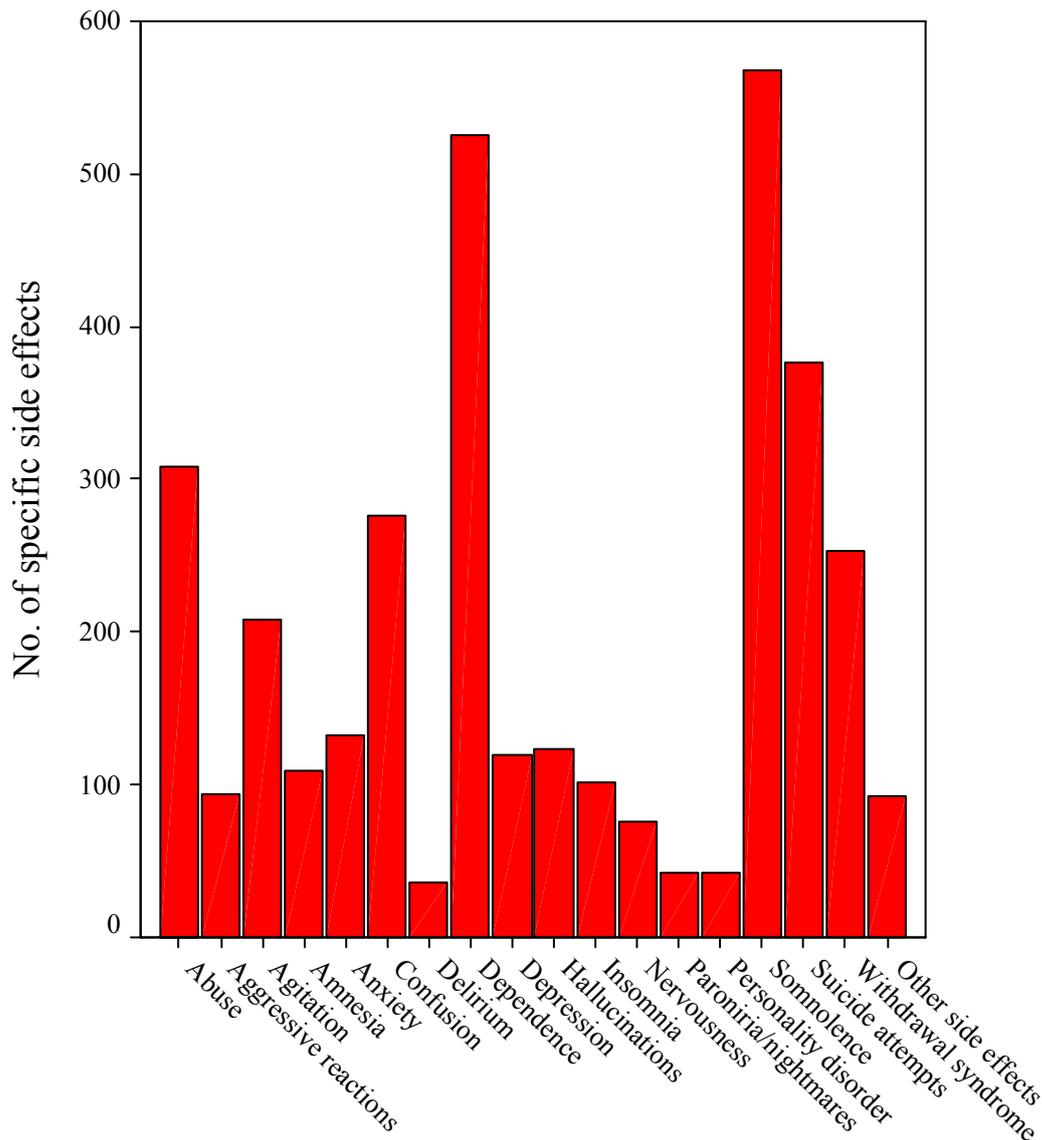
There are 2,565 spontaneous reports from general practitioners in 70 countries, including Sweden, of FZ in the World Health Organization side effects database (Bengt Lindeskog, Läkemedelsverket, personal communication, 1 July 2005) (Figure 3); the first report was recorded in 1975. Most of these reports concern mental health-related side effects (e.g., aggressive reactions, agitation, apathy, amnesia, anxiety, delirium, drug abuse, drug dependence, drug tolerance, insomnia, manic reactions, nervousness, neurosis, paroniria (“nightmares”), personality disorder, sleep disorders, somnambulism, somnolence, suicide attempts, and withdrawal syndrome). Evident psychotic-related reactions (abnormal thinking, confusion, delusions, depersonalisation, hallucinations, paranoid reactions, psychosis, schizophrenic reactions) have also been reported.



*Figure 3.* Distribution of adverse effects of flunitrazepam concerning mental health-related side effects in the World Health Organization side effects database. The first report was recorded in 1975 and the most recent in 2004.

Figure 3 shows that abuse of FZ is the most frequently reported mental health-related side effect of FZ in the World Health Organization side effects database, and research into the abuse of this compound is for this reason expedient.

For comparative purposes, spontaneous reports regarding mental health-related side effects of diazepam are also shown (Figure 4). A total of 17,198 reports of side effects from general practitioners in 70 countries, including Sweden, have been filed in the World Health Organization side effects database (Bengt Lindeskog, Läkemedelsverket, personal communication, 1 September 2005); these reports have been recorded since 1966. Figure 4 shows that dependence, somnolence and suicide attempts are the most frequently reported mental health-related side effects of diazepam in the World Health Organization side effects database.



*Figure 4.* Distribution of adverse effects of diazepam concerning mental health-related side effects in the World Health Organization side effects database. The first report was recorded in 1966 and the most recent in 2004.

Michellini, Cassano, Frare, and Perugi (1996) state that: “even though tolerance may develop to the sedative effect after approximately two to four weeks (Rickels et al. 1990), patients continue taking BZs mainly to avoid rebound insomnia and withdrawal symptoms” (p. 128). An inspection of Figures 3 and 4 gives an impression that there is a difference between FZ and diazepam in frequency of reports in this respect.

#### **Definition of FZ abuse as an example of substance-related disorders (DSM-IV)**

According to DSM-IV (American Psychiatric Association, 1994), the substance-related disorders include disorders associated with the consumption of some substance

(drug of abuse, including alcohol), to the side effects of a medication, and to toxic exposure. DSM-IV lists 11 groups of possible substances. One of these refers to sedatives, hypnotics, or anxiolytics, which, according to DSM-IV, share similar characteristics with alcohol. The substance-related disorders include two groups of disorders, the substance use disorders (substance dependence and substance abuse) and the substance-induced disorders. The later group includes several disorders that are important from a forensic psychiatric point of view, due to a possible comorbidity with, for example FZ abuse. These disorders may be relevant while studying a population of drug users: substance withdrawal, substance-induced delirium, persisting amnesic disorder, psychotic disorder, mood disorder, anxiety disorder, and sleep disorder (for a description see DSM-IV). The definition of “substance abuse” is formulated as “a maladaptive pattern of substance use manifested by recurrent and significant adverse consequences related to the repeated use of substances” (American Psychiatric Association, 1994, p. 182). *One or more* of the following criteria occurring within a 12-month period manifests substance abuse (the criteria are cited from DSM-IV (American Psychiatric Association, pp. 182-183):

- Recurrent substance use leading to clinically significant impairment or distress resulting in a failure to fulfil major role obligations at school, home or work (e.g., substance-related repeated absences from school or work, suspensions, or expulsions from school, substance-related poor work performance, neglect of children or household),
- Recurrent substance use in situations in which it is physically hazardous (e.g., driving a car or operating a machine while influenced with a substance),
- Recurrent substance-related legal problems (e.g., arrest for substance-related disorderly conduct, assault and battery, driving under the influence),
- Continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance (e.g., arguments with parent or spouse about consequences of intoxication, physical fights).

These symptoms have never met the criteria for substance dependence for this class of substance.

FZ abuse is a form of substance abuse, specifically, abuse of sedatives, hypnotics, or anxiolytics, and it may be diagnosed according to above-mentioned criteria. American Psychiatric Association (1994) indicates that substances classified as sedatives, hypnotic or anxiolytic with “rapid onset and/or short to intermediate lengths of action may be especially vulnerable to being abused” (p. 261).

### **Prevalence of FZ abuse**

The abuse of FZ is worldwide (Woods & Winger, 1997), especially in the population of drug users. It has been briefly reviewed in the *Introduction* sections of the studies included in this thesis. For references see Study I p. 85, Study II p. 28, Study III pp. 240-242, and Study IV pp. 2-3.

FZ was the most popular compound among Swedish drug users in 1996 (Sörbring, 1996). Moreover, during the period from 1997 to 2000, daily newspapers in Sweden, often in connection with reports of new cases of murders performed by offenders

intoxicated with FZ, reported that FZ is also used by 12-year-old children in school, and by high-school students, often to enhance the effects of alcohol (e.g., Wallin, 1998). The abuse of FZ by adolescents and young adults in Sweden is now a problem recognised by social workers, probation officers, medical emergency teams, prison doctors, prosecutors, customs officers, and the police (e.g., Brasing, 2002; Bratt, 2003a, 2003b; Greitz, J. Bragd, & F. Bragd, 1998; Hermansson, 1998; Lisinski, 2003, Nilsson, 1998; Vikander & Hermansson, 1998), but no epidemiological studies of FZ abuse among non-criminal adolescents, have so far been performed. Landahl (2002) performed a study on Rohypnol abuse in 82 college students (38 males and 44 females) aged between 15 and 19 years from two schools. The results showed that six male students (16% of all males) abused Rohypnol (DSM-IV) (Landahl used questions constructed by me, approximately similar to those presented in Appendix 2); no females used the drug.

Rohypnol use was first recorded in the United States in 1996. The popularity among young people is believed to depend on its low cost (less than \$5 per tablet). Walters (2005) states that it has been used throughout the United States by high-school and college students, street gang members, rave and night-club attendees, and substance abusers. The abusers are often males between 13 and 30 years, and they use Rohypnol in combination with alcohol, marijuana, cocaine, heroin, ecstasy, or LSD. A questionnaire about Rohypnol use was included in the survey entitled “Monitoring the Future” for the first time in 1996. Lifetime Rohypnol use by secondary school students in 1996 ranged from 1.5% among 8th and 10th graders to 1.2% among 12th graders. Current figures of lifetime Rohypnol use are 1.1% among 8th graders, 1.5% among 10th graders, and 1.7% among 12th graders.

### **Specific clinical effects of FZ on psychological functions and states in normal persons**

There is evidence that FZ compounds share *qualitative pharmacological properties* with other benzodiazepines (such as diazepam) (e.g., Mattila, & Larni, 1980; Stovner, Endresen, & Osterud, 1973). However, human laboratory studies have shown that FZ at therapeutic doses has *clinical effects* on several important psychological functions and states in normal subjects that differ from those of other benzodiazepines, such as diazepam. Several such clinical effects that are important from a forensic psychiatric point of view are described below.

The degree and the duration of the amnesic effect of a specific benzodiazepine may vary, and often depends on the dosage (George & Dundee, 1977), the form of administration, and the population studied (for a review see Curran, 1986, 1991; Lister, 1985). For example, Smirne et al. (1989) showed that FZ-induced memory impairment was clearly dose-related, and Bareggi, Ferini-Strambi, Pirola, and Smirne (1998) showed that memory impairment was positively associated with plasma levels of FZ. Kortilla and Linnoila (1976) have in an early study shown that an amnesic effect of FZ can be experienced without the drug affecting the level of consciousness, which may be considered desirable in preventing preoperative awareness (Mattila, Säila, Kokko, & Kärkkäinen, 1979). Kortilla and Linnoila studied 29 healthy male and female students, and defined “consciousness” as any reaction (i.e., trying to prevent

the event or moving their hands and legs) to an abdominal pinching at the time of injection of FZ. “Anterograde amnesia” was defined as an inability to remember the pinching two hours after the injection. The participants in the study were randomly allocated to one of three different dose-related groups (0.01 mg/kg, 0.02 mg/kg and 0.03 mg/kg). All participants, irrespective of the dosage, were conscious of the event, as was shown by their reacting to it, but none of them remembered the event. This result contrasts with the result from another experiment of Kortilla and Linnoila (1975) in which equivalent<sup>4</sup> dosages of diazepam were used; amnesia was shown in this study in only three out of 12 participants injected with 0.15 mg/kg of diazepam. Kortilla and Linnoila (1976) concluded that: “... in low doses, flunitrazepam has a greater amnesic action than diazepam” (p. 166).

Several later experimental clinical studies have demonstrated that FZ can cause amnesia, particularly anterograde amnesia, and that FZ is more effective in this than other benzodiazepines such as diazepam and nitrazepam (e.g., Bareggi et al. 1998; Ingum, Beylich, & Mørland, 1993; Pompéia, Gorenstein, & Curran, 1996a, 1996a; Richardson & Manford, 1979). FZ causes amnesia more effectively than a newer benzodiazepine-like compound known as “zolpidem” (Frattola, Maggioni, Cesana, & Priore, 1990).

FZ differs from other benzodiazepines regarding other clinically relevant psychological functions. It relieves anxiety before surgery effectively (C. G. Male, Lim, M. Male, Steward, & Gibbs, 1980), but it increases simple reaction time (see also below) (Farré, Terán, & Cami, 1996) and impairs co-ordination (Kortilla & Linnoila, 1976), impairs efficiency of processing information of insomniac out-patients when driving in the morning following a night-time administration of a single dose of FZ (2 mg) (Schmidt, Brendemuhl, & Ruther, 1986), lowers the performance in the card-sorting task (Bond & Lader, 1975), and modifies “normal” dream content into violent content (Gaillard & Phelippeau, 1976).

The study of Farré et al. (1996) is of a particular interest, because both triazolam (0.50 mg), and FZ (2 mg)<sup>5</sup>, compared with lower dosages of the same drugs (0.25 vs. 0.5, respectively), produced a significant impairment of the performance in the simple reaction time and lowered the number of correct responses in a digit symbol substitution test (the task was to evaluate recognition and recording of visual information), but only FZ impaired (lowered) a “balance time”. According to Farré et al. (1996) the balance task “measured the subject’s ability to stand upright on one foot with his eyes closed and arms extended to the side at shoulder height. The score for this task was the sum of the time the subject was able to remain erect without touching the raised foot to the floor when tested for 30 s on each foot; maximum possible score was 60 s (Evans et al. 1990)” (p. 4). Farré et al. concluded that FZ was “the most disruptive drug, followed by the high and low doses of triazolam and by flunitrazepam 0.50 mg” (p. 5).

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<sup>4</sup> Experimental drug discrimination studies showed that FZ is qualitatively similar to diazepam, but it is approximately 10 times more potent than diazepam (e.g., Shannon & Herling, 1983).

<sup>5</sup> It should be noted, that a therapeutic dosage of FZ is currently recommended from 0.5 to 1 mg, but during a long period after it was introduced, a dosage of 2 mg was considered as “normal” dosage (for comparison see the *Results*).

## **The association between intoxication with FZ and disinhibited behaviour (often violent)**

Teo, Chee, and Tan (1979) were among the first to emphasize FZ's potential danger, and reported five cases of young male subjects in Singapore who had made sudden, aggressive, violent attacks, directed both towards others and towards themselves (suicidal behaviour), while intoxicated with FZ. The first Swedish case of a recognised clear relationship between intoxication with FZ and violent abnormal behaviour was probably the case of a 24-year-old man, followed by the media for some days in June 1995. This young man was involved in causing serious knife wounds and gunshot wounds and taking hostages (Dåderman & Lidberg, 1999a). Following a report (Dåderman, 1996) that about 40% of male juvenile delinquents were FZ abusers, and the accompanying description of behavioural changes when intoxicated, further reports regarding a possible link between FZ and violence were searched for on Medline and PsychBase, two main sources of scientific information within the fields of psychiatry and psychology. There were no significant findings. Lack of sufficient information (lack of clear information that FZ is commonly abused with severe adverse effects, at least in some populations) was also reflected in the pharmacy compendium (FASS, 1996), an information source available at pharmacies in Sweden. Both the 1996 (FASS, 1996) and 2005 ("sök läkemedel", 2005) editions describe that: "paradoxical reactions such as a state of excitation, aggression, hallucinations, insomnia, and nightmares are uncommon (< 1/1000) during intoxication with FZ".

One report regarding aggression that had been induced by FZ was filed in 1997 in the Swedish Medical Products Agency database, which records reports from general practitioners. This was a case of an impulsive reaction and a change in personality of an elderly man who attempted to murder his wife. No new cases were reported during 1998 and 1999. One additional case of an aggressive reaction has been reported and considered as possible evidence of a link between FZ and violence since 1999, a case of a middle-aged man who maltreated his wife (Bengt Lindeskog, personal communication, 1 July, 2005). There are 23 case-study reports recorded in the World Health Organisation database about aggression and FZ during the period 1981-2004, most of them concerning aggressive reactions when patients were treated with FZ for sleep disorders (Figure 3 gives details of other mental health-related side effects of FZ in the World Health Organization database).

About 80 selected forensic psychiatric files of young men (less than 30 years old) who had been assessed at the Department of Forensic Psychiatry in Stockholm in 1991 and 1992 were studied in 1997 (Dåderman, unpublished data). This study showed that many of the violent situations occurred while the offenders were intoxicated with FZ. A series of violent crimes had been committed in several cases. It was noteworthy that the offenders in many of these cases were intoxicated with both FZ and alcohol.

Elmgren (1998), previously fellow of The Committee for Forensic Psychiatry, Social and Medical Legal Questions (Rättsliga rådet) at the National Board of Health and Welfare (Socialstyrelsen) in Sweden, has described several cases involving FZ abusers who had repeatedly committed murder, and had been admitted to forensic psychiatric evaluation (FPE) in 1993. All perpetrators were intoxicated with both FZ and alcohol at the time of their crimes. The cases were referred for forensic psychiatric

reassessment by either an investigating forensic psychiatrist or a defence counsellor, because the court was unable to agree on whether the crimes were committed under the influence of a “serious mental disorder” (see Appendix 1 for a definition). Two cases can be taken as examples. In both cases the initial FPE had reached the conclusion that the perpetrator was not suffering from a serious mental disorder when the crimes were committed. One subject, E, was charged with attempted murder following an unprovoked, frenzied attack on a stranger. E remembered nothing of the event, which had taken place while he was under the influence of 1½ tablet of Rohypnol and a small amount of alcohol. The initial FPE had diagnosed him borderline personality disorder and dependence on anxiolytics. The reassessment diagnosed mental disorder with several serious symptoms. In particular, it emphasised that E was close to psychosis when he committed the crime, as he had also been when contacting the psychiatric services before the crime. Another man, F, committed murder. Again, the initial FPE had found that F was not suffering from a serious mental disorder at the time of the crime. The reassessment emphasised F’s dependence on alcohol and benzodiazepines, and the breakdown of his weak personality when under the influence of these substances. The reassessment decided that the crime was an impulsive outbreak of aggression based on an uncomplicated self-inflicted intoxication. There were no psychotic symptoms when the crime was committed and the reassessment decided that F did not suffer from a serious mental disorder at the time of the crime.

Two unpublished reports became available in 1999, one of them prepared in the United States by the Drug and Chemical Evaluation Section Office of Diversion Control (DEA, 1996), which resulted in FZ being rescheduled as a Schedule I preparation (the same schedule as heroin and LSD); and the other (Dobbin, 1997) prepared by Dobbin for the Australian National Drugs and Poisoning Scheduling Committee at the Department of Human Services, which resulted in FZ being rescheduled as a Schedule 8 preparation (the Australian schedule that includes drugs of addiction). The later report includes descriptive information from juvenile justice workers about their impressions and experiences with FZ abuse by juvenile delinquents in Australia.

Dobbin (1997) reviewed drug reaction reports that had been received by the World Health Organization’s Collaboration Centre for International Drug Monitoring, Uppsala, Sweden. The reports included a survey from a Belgian general practitioner of a group of his methadone patients. This general practitioner described the effects of FZ as “a state of euphoric excitement, disinhibition, and a feeling of invincibility (which the author calls ‘the Rambo effect’)”, “uncontrollable paranoid aggressiveness sometimes occurred, leading to criminal violence of which the users remembered little if anything” (Dobbin, 1997, p. 6).

Dobbin (1997) cited a German report that stated that two-thirds of German heroin addicts are also addicted to FZ. These addicts suffer from anterograde amnesia when intoxicated with FZ, and they behave in a criminal, aggressive and self-destructive manner. In Scotland, drug abusers found FZ to be a “better” and “stronger” alternative to temazepam, and it is widely abused by intravenous injection. Rohypnol is known in Scotland as “wallbangers” (Institute for the Study of Drug Dependence, 1995).

Dobbin (1997) described reports regarding the abuse of FZ by offenders from South Australian prisons, which commented that: “although most prisoners pose few direct threats to staff, those who take Rohypnol (known as Rambo pills) often display violent and aggressive behaviour, and seem to be possessed of enormous strength” (p. 23). Dobbin attached several opinions from medical and other professionals about FZ to his report. One general practitioner in New Zealand said: “Rohypnol was withdrawn from the New Zealand market at the time when it was associated with motorcycle gangs and violence”; and another general practitioner in Victoria, Australia, said: “Rohypnol is the drug which causes the most problems. Individuals get aggressive, and don’t remember their actions, and end up in jail”; while another said: “Rohypnol causes the most problems. It causes the patients to become aggressive, ‘off their head’. Also rapid talking, disinhibited behaviour”. A specialist in alcohol abuse and drug abuse said: “Rohypnol is mentioned considerably more frequently than other drugs for its involvement in crime causing referral of individuals to the present Unit for assessment, particularly violent crimes or reckless criminal behaviour. It is associated with aggression. The street name ‘Rambos’ characterises the effect it has on individuals giving them the courage required to commit burglary and other crimes” (p. 39-40).

Dobbin (1997) also described several cases of violent behaviour in juvenile delinquents when intoxicated with FZ, and a social worker said: “It is called the ‘crime drug’ because you can take a few, do things you wouldn’t normally do, and you won’t remember” (p. 43).

The Swedish National Board of Forensic Medicine investigated the extent and character of benzodiazepine use and abuse in 2001. I was among the researchers who initiated the project among Swedish offenders, which has resulted in a book, entitled *Lugnande medel som oroar* [Sedative substances that make us anxious] (Holmberg et al. 2002). A total of 583 subjects undergoing a “minor” FPE (see Appendix 1), and 416 subjects on remand at the detention centres in Göteborg, Huddinge, and the Kronoberg Prison in Stockholm participated. The project examined the prevalence of FZ abuse and the abuse of other benzodiazepines (and two newer benzodiazepine-like compounds, zolpidem and zolpiclone). We found that 13% of the participants had committed the crime that led to detention or the FPE while under the influence of some type of benzodiazepine compound; the use of benzodiazepines was more frequent in younger participants (16-25 years) than in those above the age of 25 years; offenders who were accused of aggravated assault and robbery (including robbery with the use of violence) were more frequently under the influence of benzodiazepines than those who did not commit such crimes; 87% of those who were intoxicated with benzodiazepines while committing their crimes were polysubstance abusers; 85% obtained the drug illegally. This project includes several studies; one of them reviewed the literature on violent behaviour and other adverse effects of FZ intoxication (Dåderman, 2002a). Another study (Holmberg & Dåderman, 2002; Dåderman, Holmberg, & Ingerloo, 2002) describes in detail ten cases of FZ abusers undergoing an FPE during 2001 and their violent crimes. None of the cases was considered to be suffering from a serious psychiatric disorder, and thus none of them received forensic psychiatric care. The cases of FZ intoxication during the crime exemplify clearly an association between intoxication with FZ and the brutality of violent acts and

impulsiveness, and they exemplify a temporary personality change in the offenders while intoxicated.

### **Basic concepts in neuropsychopharmacology**

Studies within neuropsychopharmacology focus on how drugs affect the nervous system and behaviour (the Greek word *pharmakon*, which is the root of “pharmacology”, has three different meanings: “a charm”, “a poison”, and “a remedy or medicine”). It is necessary to understand how nerve cells conduct signals in order to understand how drugs affect the brain and change behaviour (see Kalat, 1995), because, according to Kalat “each neuron synthesizes its neurotransmitters from materials in the blood” (p. 68).

Nerve cells (neurones) are specialised for receiving, processing, and transmitting signals. Kalat (1995) defines neurotransmitters as “the chemicals released at the synapse” (p. 68). Nerve impulses (called action potentials) are propagated changes that travel rapidly along the axons of neurones by means of a chain reaction. Local potentials, on the other hand, (also known as graded potentials or post-synaptic potentials) are propagated nerve impulses, initiated at post-synaptic sites that travel the length of the axon without diminishing in amplitude. Cell bodies process information by integrating (adding) post-synaptic potentials across their surfaces. Neurones communicate with other neurones at synapses. Some synapses use electrical transmission to affect a post-synaptic cell, while others require a chemical transmitter (signal) to be released from a neurone. Most synapses require a chemical transmitter that diffuses across the extremely narrow space between pre-synaptic and post-synaptic cells, and binds to receptor molecules in the post-synaptic membrane. At some synapses, the receptor molecule responds to a neurotransmitter by opening an ion channel within its own structure, while at other synapses the binding of a transmitter molecule to a receptor molecule leads to the opening of channels by the activation of G-proteins and second messengers (the interested reader may see Stahl, 2005, who provides a very clear description of the formation of an intracellular second messenger). Thus, the “first messenger” (neurotransmitter) sends the message to the postsynaptic cell’s receptor. The first messenger causes the receptor to change in such a way that a G-protein is able to bind to the receptor. When the G-protein is bound to the receptor, its shape changes such that the G-protein can bind to an enzyme. The enzyme now can synthesize a “second messenger”. The second messenger sends a message to several areas inside the postsynaptic cell. The second messenger may open or close an ion channel in a membrane or change the production of proteins or the structure of the postsynaptic cell.

According to Kalat (1995) “the meaning of a neurotransmitter depends on the receptor that receives it” (p. 73).

The relationship between the number of excitatory and the number of inhibitory signals received by a neurone determines whether the neurone fires off an action potential at any given moment (Kalat, 1995; Rosenzweig, Leiman, & Breedlove, 1999). Some neurones and some synaptic transmitter chemicals are specialised to send inhibitory messages. An example of an inhibitory chemical is the synaptic neurotransmitter gamma-aminobutyric acid (GABA), which is the major inhibitory

neurotransmitter in the central nervous system (CNS) (for a review see Korpi, Gründer, & Lüddens, 2002). Korpi et al. state that inhibition is a fundamental brain process and that GABAergic mechanisms are directly associated with all physiological and behavioural processes, and are also involved in many neuropsychiatric illnesses.

### *How do benzodiazepines affect the brain?*

Kalat (1995) describes how “like many other drugs, benzodiazepines were found to be effective long before anyone knew how they work” (p. 434). The specific benzodiazepine receptors in the CNS to which benzodiazepines (and alcohol, barbiturates, and other compounds) bind (see e.g., Sandford, Argyropoulos, & Nutt, 2000, p. 204, Figure 1; Rosenzweig et al. 1999, p. 95, Figure 4.12), were, according to Kalat, discovered in the late 1970s and early 1980s.

The different pharmacological and therapeutic properties of the different benzodiazepines are assumed to be related to their specific affinities for the GABA receptors. Research on how benzodiazepines act has revealed that they bind with high affinity<sup>6</sup> to specific binding sites located on the GABA<sub>A</sub> receptor complex system (see e.g., Kalat, 1995, p. 435, Figure 12.10) in the CNS. The various benzodiazepines have different affinities for these binding sites, and different efficacies (an ability of achieving the intended result) when bound (Tallman, 1981). Both affinity and efficacy are examples of *pharmacodynamic* properties. Möhler and Okada (1979) postulated that the brain contains a physiological ligand (a substance that binds to receptor molecules, such as those at the surface of the cell) for these benzodiazepine receptors. Rosenzweig et al. (see 1999, p. 95, Figure 4.12) emphasize that: “the benzodiazepine does not bind to the same site on the receptor as does the transmitter GABA” (p. 94).

The effect of benzodiazepines depends on the level of activity of GABA systems, which may explain some exceptional reactions to benzodiazepines in elderly patients and in children (for a review see Tallman, 1981). The possibility of decreasing neuronal activity following activation of GABA<sub>A</sub> receptor complex has been the focus of pharmacological manufacturers, who have developed benzodiazepines, and who have also developed other compounds in recent years (see Table 1).

GABA receptors are divided into three major classes (“receptor complex systems”) (GABA<sub>A</sub>, GABA<sub>B</sub>, and GABA<sub>C</sub>), each one with different properties (Kalat, 1995). Receptors in the GABA<sub>A</sub> class (see e.g., Kalat, 1995, p. 435, Figure 12.10) are ionotropic receptors (which means that they contain a chloride channel and can react quickly). Compounds that act on GABA<sub>A</sub> receptors rapidly alter brain functions (Basile, Lippa, & Skolnik, 2004). Benzodiazepines, and the newer benzodiazepine-like compounds (see Table 1), act only as promoters of the action of GABA on the GABA<sub>A</sub> complex of receptors. The brain has a large amount of different types of GABA receptor “aggregate”, through mixing of different subunits (Miczek, Fish, & De Bold, 2003), whose expression varies in different cells and brain regions. Korpi et al. (2002)

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<sup>6</sup> According to Rosenzweig et al. (1999), “the compound that binds to the receptor longer is said to have a greater binding affinity (or simply, affinity) for the receptor” (p. 89). Rosenzweig et al. explain that “if the drug has a very high affinity (and therefore binds to the receptor for a relatively long time), then a very low concentration of drug molecules will be sufficient to bind half the receptors present. So pharmacologists tend to speak of a drug’s affinity for the receptor in terms of the concentration of drug needed to bind half the receptors. The lower this concentration is, the greater the drug’s affinity” (p. 89).

claim that the diverse pharmacological proprieties of these receptor subunits in different brain cells and brain regions create an opportunity to target receptor subunits with novel drugs.

### *A brief introduction to neurotransmitters and their functions*

Most sleep-inducing drugs, including benzodiazepines, bind strongly to receptors, which appears to enhance the activity of a subset of receptors for the inhibitory transmitter GABA (Nutt, Adinoff, & Linnoila, 1988). It results in the production of more inhibitory postsynaptic potentials than it should be possible to produce by GABA alone (for a review see Korpi et al., 2002; Rosenzweig et al., 1999). A brief introduction to the different synaptic neurotransmitters (see e.g., Kalat, 1995; Rosenzweig et al., 1999; Sternberg, 2004) on which the GABA system exerts inhibitory effects (see Kenyon, 2005) and their pathways, provides an understanding of how benzodiazepines (including FZ) may act.

*Acetylcholine* was the first chemical substance that was discovered to act as a neurotransmitter, in investigations of the frog heart by Otto Loewi (a German physiologist) in 1920 (Rosenzweig et al., 1999). Nerve cell bodies containing acetylcholine are called cholinergic. Cholinergic cells are located mainly in the hippocampus and the amygdala. Kalat (1995) provides evidence that “electrical stimulation of amygdala can lead to vigorous affective attacks” (p. 440). The hippocampus plays a role in memory for facts (Rockland, 2000), while the amygdala plays a role in emotions (anger and aggression) (Canli, Sivers, Whitfield, Gotlib, & Gabrieli, 2002). The main functions ascribed to cholinergic pathways are related to arousal, learning or memory, and motor control (Rosenzweig et al., 1999). The most important role of cholinergic pathways is in the processes of learning and memory. Rosenzweig et al. have suggested a behavioural role of acetylcholine in the regulation of sleep and in the control of some aspects of sleep states.

*Dopamine* plays a role in movement, attention, and learning; it is also involved in pleasurable responses (Sternberg, 2004). Dopaminergic neurones are located in several regions of the brain, including the mesostriatal system, which includes the olfactory tubercle and which is implicated in motor control; and the mesolimbic system (Rosenzweig et al., 1999), which projects to the limbic system and the cortex and which mediates behavioural effects that are thought to be important to reward mechanisms and to maintenance of mental homeostasis. Degeneration of the mesostriatal system, through loss of neurones either with ageing or drug abuse (such as the abuse of stimulants such as amphetamine derivatives), can result in severe motor dysfunction, such as Parkinson’s disease. It is thought that an over-stimulation of mesolimbico-cortical dopamine systems is related to schizophrenia and other psychotic disorders.

Neurones that release *noradrenaline* (Rosenzweig et al., 1999) extend broadly throughout the cerebral cortex, limbic areas, hypothalamus, cerebellum and the spinal cord. These neurones are believed to modulate many behavioural and physiological processes. Some of the more important ones are mood systems and reward systems, arousal, blood pressure and neuroendocrine regulation.

*Serotonin* (5-hydroxytryptamine, 5-HT) plays a role in arousal and sleep, in mood changes, hallucinations, appetite, the control of sensory transmission, and sensitivity to pain (Rockland, 2000; Sternberg, 2004). We have a comparatively low number of neurones which release serotonin. Large areas of the brain are innervated by relatively few serotonergic fibres, which are concentrated in the brain stem, most of them in what are known as “raphe” nuclei near the midline. An important serotonergic pathway that is involved in the control of different sleep stages emerges from the dorsal raphe nuclei. More than 15 types of serotonin receptor have been described. The diversity of receptors and pathways that underlie the varied electrophysiological actions of serotonin, together with the differential expression of these receptors in different neuronal populations, may explain how it is possible for one transmitter to be linked to such a large array of behaviours, clinical conditions, and drug actions. For example, changes in serotonin function have been noted in affective disorders, anxiety states, schizophrenia, obsessive-compulsive disorder, eating disorders, migraine, and sleep disorders.

The most common neurotransmitters in the brain are amino acids (Rosenzweig et al., 1999; Sternberg, 2004). There are two such groups, excitatory amino acids (e.g., *glutamate* and *aspartate*), and inhibitory amino acids (e.g., *GABA* and *glycine*) (Kalat, 1995). According to Sternberg (2004) GABA “is synthesized from glutamate” and it “seems to have direct inhibitory effects on axons; it thereby lowers the threshold of excitation” (p. 77). These transmitters are distributed throughout the CNS. GABA is an inhibitory transmitter (Kalat, 1995) that reduces activity in broad regions of the brain, especially in the parts of the brain that are responsible for arousal (such as the limbic system, which is also responsible for emotions and empathy). GABA activates both ionotropic (GABA<sub>A</sub>) and G-protein-coupled (GABA<sub>B</sub>) receptors.

### **Neuropsychopharmacological properties of FZ**

FZ has the chemical abstract name of 5-(2-fluorophenyl)-1,3 dihydro-1-methyl-7-nitro-2H-1,4-benzodiazepin-2-one. Other names include 1-methyl-7-nitro-5-(2-fluorophenyl)-3H-1,4-benzodiazepin-2(H)-one and Ro 5-4200. FZ has a molecular weight of 313.30 and the chemical formula C<sub>16</sub>H<sub>12</sub>FN<sub>3</sub>O<sub>3</sub> (DEA, 1996). FZ is a benzodiazepine that produces sedative-hypnotic (sedative drugs, also called anxiolytics, are used to relieve states of anxiety; while hypnotics are used to produce drowsiness and sleep), anticonvulsant, and muscle-relaxant effects. It also has special clinical uses for the induction of anaesthesia, and for sedation prior to surgery (Mattila & Larni, 1980). The hypnotic effects of FZ tend to be stronger than the anxiolytic, muscle-relaxing and anticonvulsant effects.

Traditional drug abusers want to achieve the desired neuropharmacological effect as rapidly as possible, and they want it to last for as long as possible (Farre & Cami, 1991).

#### *Pharmacokinetic properties of FZ*

FZ has typical benzodiazepine effects, with a potency that is greater than that of the reference benzodiazepine, diazepam (DEA, 1996). The DEA study reviews several

early animal and clinical studies that were conducted to examine this issue. “Potency” was defined as the magnitude of the ability to cause anticonvulsant, sedative/hypnotic, muscle relaxant, discriminative stimulus, and anxiolytic effects of the substance. The reviewed studies showed that the relative weight-for-weight potency of FZ was about 10 times higher than that of diazepam. This potency, however, was not the same for all effects of FZ.

The pharmacokinetic properties are important properties that determine the abuse liability of a drug. It is generally believed that the *rate of onset of action* is more important than the duration. FZ is lipid-soluble, which contributes to its rapid uptake into brain tissue and the rapid onset of its effect on the benzodiazepine receptors. FZ can be taken orally, by injection and by inhalation. About 40% of FZ abusers in Germany take FZ via injection (Keup, 1995). An intranasal method of administering FZ (FZ tablets are ground up and inhaled) is usual among slum-adolescents in Chile (Maddaleno, Florenzano, Cruz, & Vidal, 1988). The onset of action is much faster when using injection or inhalation than after oral administration, and the possibility of using these methods of administration is a critical aspect of the abuse liability of a drug.

How is the subjective effect of the rate of onset of action of a benzodiazepine compound measured? The rate of absorption from the gastrointestinal tract after oral administration is one property that can be measured. The rate of absorption of FZ is generally quite high, much higher than those of oxazepam, estazolam, halazepam, and prazepam (Busto, Bendayan, & Sellers, 1989; Greenblatt, 1985). It is slightly lower than that of midazolam, and approximately the same as those of alprazolam, diazepam, flurozepam, lorazepam, and triazolam (Busto et al., 1989; Jochemsen, van Boxtel, Hermans, & Breimer, 1983) (see also Table 1). Aaltonen et al. (1981) administered FZ both by intravenous injection and by oral administration. They used gas chromatography to measure FZ concentrations in blood and showed that FZ rapidly crosses the blood/brain barrier and appears in detectable quantities in the cerebrospinal fluid (CSF). The FZ concentration in the CSF is 2.8% of the level found in plasma within five minutes of intravenous injection, which is a much faster rate of action than chlordiazepoxide and lorazepam.

Another pharmacokinetic property is the *duration of action* of a drug. This can be determined by measuring the rate of metabolism, by looking for the existence of active metabolites, or by measuring the rates of distribution into and out of the brain. FZ is metabolised to a number of metabolites [including norflunitrazepam, desmethyl-flunitrazepam (Ro 05-4435), and a principal metabolite 7-aminoflunitrazepam (Ro 20-1815)], two of which are biologically active and are believed to contribute to the pharmacological effects observed after FZ administration. More than 80% of a dose of FZ is excreted via the urine and the remainder via the faeces. Less than 0.2% of an FZ dose is excreted as unchanged drug. At least 11 metabolites of FZ have been observed in urine. The average half-life of FZ in plasma is about 25 hours, with a range between 15 and 66 hours (Grahnén, Wennerlund, Dahlström, & Eckernäs, 1991; Jochemsen et al., 1983; Kangas, Kanto, & Pakkanen, 1982) (Table 1 gives data presented by the World Health Organization). The actual duration depends, however, on the dose of FZ that is administered. It is also believed that the duration is related to many individual factors, such as the number of central receptors, the age and gender of an FZ abuser,

and whether it is taken in combination with other substances. In addition, norflunitrazepam and 7-aminoflunitrazepam, which are active metabolites of FZ, appear slowly and reach maximum concentrations that are less than that of FZ itself. They are still present in high concentrations 24 hours after a single dose of FZ. With chronic administration, accumulation of FZ occurs in plasma and lesser concentrations of the two active metabolites of FZ are found.

### *Pharmacodynamic properties of FZ*

FZ has a nitro-group and a fluorine atom in the molecule, both of which increase the hypnotic effect. FZ acts as other benzodiazepines and enhances the transmission of GABA into the CNS by special benzodiazepine receptors. GABA has an inhibitory effect on many important neurotransmitters, such as noradrenaline, serotonin, dopamine, and acetylcholine.

In the case of receptor pharmacology, Squires and Braestrup (1977) have shown that FZ binds with high *affinity* to benzodiazepine receptors in rat brain with a potency that is equivalent to that of clonazepam and approximately seven times greater than that of diazepam. FZ has much greater affinity to the benzodiazepine receptor than clobazam; a greater affinity than diazepam, oxazepam, and alprazolam; and a lower affinity than midazolam and triazolam (Arendt, Greenblatt, Liebisch, Lun, & Paul, 1987; Braestrup & Squires, 1978). FZ has a greater *efficacy* for producing changes in the electroencephalogram (EEG) and in blocking of seizures than midazolam, oxazepam, and clobazam (Laurijssens & Greenblatt, 1996; Mandema, Sansom, Dios-Vieitez, Hollander-Jansen, & Danhof, 1991). FZ thus has high values of the two pharmacodynamic variables affinity and efficacy.

In summary, FZ is a sedative-hypnotic benzodiazepine with a rapid onset of action and intermediate duration of action (pharmacokinetic properties) (see Table 1, Note no. 1 for the definition presented by World Health Organization, 1996), with high affinity to, and with high efficacy at, central benzodiazepine receptors (pharmacodynamic variables).

### **A biological “vulnerability model” of deviant behaviour**

No behaviour can occur without an underlying mechanism and no person operates in a vacuum. We behave in response to our environment – for example, in response to cultural or social rules, psychoactive substances, or stress.

It is known that platelet monoamine oxidase (MAO) is associated with the central serotonergic function (Oreland & Shaskan, 1983). Buchsbaum, Coursey, and Murphy (1976) formulated the biological vulnerability hypothesis. According to this hypothesis, a low activity of platelet MAO is associated with certain personality traits. These traits in turn are associated with a predisposition to psychiatric or psychological vulnerability. Such constitutional vulnerability predisposes people with certain personality traits to breakdown in the presence of stress or somatic disease. Support for this hypothesis was provided by the findings of Coursey, Buchsbaum, and Murphy (1982), Schalling, Åsberg, Edman, and Oreland (1987), and Virkkunen et al. (1994). Platelet MAO activity is low in male subjects who show high ratings for sensation

seeking, extraversion, impulsiveness, and (to a lesser degree) aggression (Stålenheim, von Knorring, & Oreland, 1997; for a review see Oreland, 1993, 2004, and Oreland et al., 2004).

### **Theories of personality traits**

An important research issue is whether persons who share several common behavioural characteristics (e.g., male offenders) have personality characteristics in common. Vulnerability to abuse may well be increased by a deviant pattern of personality traits. If substance abusers are a heterogeneous group, with some motivated by, for example, high temperamental sensation-seeking needs, while others are driven by impulsiveness or aggression, a better understanding of these motivations can lead to more effective strategies of prevention and early identification of “poor responders” within different treatment programs, according to etiology.

New-borns differ in activity level and irritability, and adolescents and adults differ from one another in many respects. More than 2,000 years ago, the Greek writer Theophrastus asked: “Why is it that while all Greece lies under the same sky and all Greeks are educated alike, yet we all have characters constituted differently?” The theory of the four temperaments (phlegmatic, choleric, melancholic, and sanguine), conceived by Hippocrates in the 5th. century BC and further developed by Galen in the 2nd. century AD, hypothesised that personality differences are related to the composition of body fluids.

Personality traits are seen as relatively stable characteristics of a person that cause this person to behave in a particular way with cross-situational consistency. Personality traits are not unstable states. (A “state” is a particular type of behaviour that only exists temporarily). For example, a person with trait “anxiety” is not always in a state of anxiety (feelings of fear and tension accompanied by autonomic nervous system arousal), but has a disposition to react with anxiety when exposed to stress or unpleasant situations.

#### *Sjöbring’s theory*

As early as 1919, the Swedish psychiatrist Henrik Sjöbring formulated systematic theories of personality structure, based on observations on psychiatric patients (Sjöbring, 1958/1973). His theory included three major personality traits: *validity*, *solidity*, *stability*, with the addition of *capacity* to describe the person’s intellectual capacity. Capacity was an important trait in the psychiatric or psychological assessment of a person.

Sjöbring assumed that personality traits are developmental. He distinguished between a normal variation (genetically determined), and a lesional variation (caused by trauma, infection, or other pathological reasons). He observed that changes from normal to deviant behaviour could be related to brain damage. He assumed that very low values of the personality traits validity and solidity, which he used the prefix “sub” to denote, are signs of psychiatric deviance or predisposition to such deviance. On the other hand, “sub-stability” would indicate mental health rather than disorder (see below). Very high values, denoted as “super”, are signs of mental health and

therefore indicate successful social inter-relations. He further assumed that personality traits are normally distributed within the population, as is capacity (intelligence scores, IQ).

A “sub-valid” person has relatively low self-esteem, and shows properties that characterise psychasthenic neurotic patients (easily tired, tense, irritable, emotionally labile (“ambivalent”) and meticulous). A “super-valid” person has relatively high self-esteem with a good self-knowledge, has a tendency to show persistent, calm, unafraid and enterprising behaviour.

A “sub-solid” person is hysteroid and prone to primitive reactions, and impulsive. A “super-solid” person is objective, unchangeable, independent, “rigid”, and nonimpulsive (controlled).

A “sub-stable” person is sociable and trustworthy, with intense and warm feelings. Such a person uses a low level of abstraction, and is focused on concrete reality. He or she is vulnerable to environmental stress. A “super-stable” person has an elegant and swift lifestyle, is high in abstraction, and does not care about other people’s feelings. Thus, “super-stability” reflects a tendency to show a sophisticated, skilful and emotional distance towards other people, indicating detachment and low empathy.

The construction of the Marke-Nyman temperament (MNT) inventory was based on Sjöbring’s theory (see *Methods*). The MNT inventory has been the most frequently used method used to define Sjöbring’s personality traits in practice. The MNT was used in the early 1970s on a sample of male offenders undergoing an FPE, and its relationship to some biological correlates was studied (Levander, Schalling, L. Lidberg, Bartfai, & Y. Lidberg, 1980; L. Lidberg, Levander, Schalling, & Y. Lidberg, 1978). Engström, Alling, Gustavsson, Orelund, & Träskman-Bendz (1997) studied personality profiles in relation to biological parameters (platelet MAO activity and cortisol) in suicide-attempters. Recently, Lindström et al. (2004) published a study in a group of suicide attempters. They found that the patients had higher scores on the MNT stability scale (patients were characterized by super-stability) than control subjects (healthy persons, mainly hospital staff). They also found that the whole brain binding potential of the serotonin transporter (5HTT) was associated with impulsiveness (i.e., a positive correlation between scores on the MNT solidity scale and 5HTT) in the patient group (and not in controls).

#### *Eysenck’s theory and comments regarding his unitary construct of cortical arousal*

Hans J. Eysenck, a leading British psychologist, formulated in 1967 a trait theory based on a biological foundation (mainly on cortical arousal), and included three major personality traits: extraversion, neuroticism, and psychoticism. These three traits are statistically independent and uncorrelated. Eysenck assumed that individual differences in optimal levels of stimulation and cortical arousal contribute to the development of different strategies. People with high values of extraversion tend to be under-aroused in non-stimulating conditions, and thus become more active and seek more stimulation in order to reach higher levels of arousal. People with high values of neuroticism react with strong emotions in situations that normally would not elicit such affective intensity. Eysenck related psychoticism to the level of androgens. The relationship between psychoticism and androgens has yet to be investigated, and the

validity of the construct of psychoticism is still unclear. It is commonly assumed that people with high values of psychoticism are solitary and lack feelings, caring, empathy, and sensitivity, and that they are often detached in their relationships with others. According to Eysenck (1975), offenders are characterized by psychoticism.

Eysenck's *unitary* construct of cortical arousal (Eysenck, 1982) has outlived its usefulness, because it is possible to separate cortical arousal into small arousal sub-systems corresponding to a similar chemical differentiation of the reticular formation of the brain (Robbins, 1997). It is also possible, according to Robbins, that attention, stimulus-processing, and arousal are influenced by neurotransmitter systems independent of each other; the coeruleo-cortical noradrenaline system seems to have a protective function in stressful or arousing situations; the mesolimbic and mesostriatal dopamine systems appear to play a role in the activation of cognitive or motor output; the cholinergic systems enhance stimulus processing (attentional selection, discrimination learning and spatial working memory) at the cortical level; the serotonin system contributes to behavioural inhibition and cortical de-arousal.

Eysenck's personality traits may be measured by different versions of self-report inventories (see *Methods*), and research suggests that Eysenck's personality traits predict health outcomes.

#### *Zuckerman's psychobiological model of sensation seeking*

The study of the sensation-seeking trait (Zuckerman, 1994) is based on studies concerning individual differences in reactions to sensory deprivation (Zubek, 1969). Sensory experiments showed that rodents, monkeys, and humans deprived of patterned stimulation developed what is termed a "drive for stimulation", a drive for the reinforcement of external stimulation, even if such stimulation was meaningless and unrelated to primary drives. Animal research has suggested that this is a vulnerability trait for drug dependence. The behavioural characteristic of this vulnerability is hyperactivity in response to a novel environment. Zuckerman widened this perspective to a broad sensation-seeking trait, defined by him (1979, p. 10) as "the need for varied, novel, and complex sensations and experiences, and the willingness to take physical and social risks for the sake of such experiences". Zuckerman was particularly interested in the biological bases of sensation seeking, and performed many experiments with animals to test his assumptions. The first theory of sensation seeking was, like Eysenck's theory of extraversion, based on arousal. The sensation-seeker was assumed to be habitually under-aroused. Zuckerman later left the arousal concept and proposed that sensation seeking is related to the levels of central monoamines, in particular levels of the catecholamines and their enzymes. This means that sensation seeking is a dysfunction of the central serotonergic system, easily measured by measuring the levels of platelet monoamine oxidase (MAO) (Zuckerman, 1993). Sensation seeking has emerged as an important explanatory construct for a variety of behaviours, including criminality and the use of alcohol and illegal drugs (Newcomb & McGee, 1991).

Zuckerman's personality traits may be measured by different versions of self-report inventories, where the Sensation-seeking scale, Version V (SSS-V) has been the

most frequently used method to discover the sensation-seeking construct in practice (see *Methods*).

### *Schalling's and her co-worker's theories*

Daisy Schalling, a leading Swedish psychologist, formulated, together with her co-workers (Schalling, Cronholm, & Åsberg, 1975), a trait theory based on a biological foundation: physiological correlates and transmitter substances in the brain. Schalling and her group were particularly interested in biological and cognitive measures, and have performed many experiments with patients and healthy subjects to confirm these correlates (Edman, Schalling, & Levander, 1983; Edman, Åsberg, Levander, & Schalling, 1986; Schalling, Edman, & Åsberg, 1983; Schalling & Åsberg, 1985; Schalling et al., 1987). Schalling et al. (1975) also formulated a two-factor theory of anxiety, based on previous research (Buss, 1962). This theory explains the personality trait of anxiety in terms of two kinds of anxiety, somatic anxiety (autonomic disturbances, distress, and panic) and psychic anxiety (worry).

### **Personality traits that are related to the abuse of alcohol and drugs**

Several studies have indicated that there is a link between some personality traits and drug abuse and alcohol abuse (Tables 2-4 give references regarding personality traits assessed in the studies included in the present thesis), while other studies have claimed that the search for a unitary “addictive personality” has not been especially fruitful (Nathan & Lansky, 1978; Pihl & Spiers, 1978). Studies investigating the relationship between serotonergic and dopaminergic transmission and personality traits have suggested that the transmitter system is involved (for a review see Orelund, 1993, 2004). Nobody lives in a vacuum and the etiology of several personality disorders (such as antisocial personality disorder and borderline personality disorder) is probably multifactorial (for a review see Gabbard, 2005). Most of the offenders studied during the work reported in this thesis had been diagnosed with personality disorders, and thus this perspective must be kept in mind.

The first study on the SSS and different drug use was reported by Zuckerman, Bone, Mangelsdorff, and Brustman (1972) (see Galizio & Stein, 1983, for a review of early findings). Sensation seeking is predictive of early drug use (Newcomb & McGee, 1991). Studies on criminal men have shown that they score higher than non-criminals on all sensation-seeking subscales, with one exception (Haapasalo, 1990; Dåderman, 1999). The exception is the thrill-seeking and adventure-seeking scale (see *Methods*), where offenders score significantly lower than nonoffenders. These results indicate that men involved in criminal acts have a need to take social and legal risks, but this need is not expressed in participation in physically risky activities or sports. Studies of men (Rydellius, 1983) and women (Hallman, von Knorring, Edman, & Orelund, 1991) who abuse alcohol show that the personality pattern of alcoholics is characterised by higher scores than nonabusers on the impulsiveness, monotony-avoidance (sensation seeking), and somatic anxiety-related scales, and by lower scores on the socialisation scale.

A factor associated with abnormal behaviour is a low level of social conformity, measured by the socialisation scale from the KSP. This has been extensively studied both in healthy subjects and in forensic patients (for a review see Gustavsson, 1997). Criminal and non-healthy patients achieve very low scores on the KSP socialisation scale. Studies suggest that awareness of personality traits may be crucial for a better treatment outcome in drug users (e.g., Stenbacka, Brandt, & Lettholm, 2004).

I have carried out a very brief review of relevant studies, those that present predictive and discriminant validity with respect to substance abuse, with the focus on the validity of self-report inventories. I identified these studies by conducting thorough searches in Medline only, using combinations of the term “substance abuse” with the terms “Marke-Nyman temperament inventory”, “Eysenck Personality Questionnaire”, “sensation seeking scale”, and “Karolinska Scales of Personality”. The search on the Marke-Nyman temperament inventory did not find any studies, indicating that the MNT has not been validated in the population of people with substance use disorder. An analysis of the results presented in Tables 2-4 indicates that the scales, based on the theories described above, have good discriminant validities in the population of people with substance use disorder. There is one exception: MNT, for which the validity of the scales included in this inventory, has not been examined.

Table 2

*Studies on the predictive and discriminant validity of Eysenck's Personality Questionnaire (EPQ) with respect to substance abuse*

Study	Participants	Main findings
Gerra et al. (2004)	1,076 urban Italian high school students aged 14 to 19 years. Lifetime alcohol use was found in 81%, "alcohol abuse" in 38% (multiple drug users), cannabis use in 26%, ecstasy in 3%, heroin in 4%, and cocaine in 8%.	"Minimal experimenters" scored higher than nonusers on the EPQ P scale, but lower than "habitual" drug users.
Roy (2003)	280 American alcoholics; 43% of them had attempted suicide and these participants had higher scores for emotional abuse, physical abuse, sexual abuse, emotional neglect and physical neglect.	Alcoholic suicide attempters scored lower than non-attempters on the E scale and higher on the EPQ N scale.
Semple et al. (2003)	10 regular cannabis users and 10 healthy controls, matched for age, sex, and premorbid IQ. Cannabis users used significantly larger amounts of alcohol.	A positive relationship was found between the EPQ-R P scale and cannabis, tobacco, and alcohol use.
Saiz et al. (2003)	2,862 secondary school students in Oviedo (Asturias, Northern Spain), aged 14 to 17 years, 51% males. The prevalences of lifetime, previous year and previous month cocaine use were 6%, 5% and 3%, respectively. Cocaine ranked sixth among illicit drugs ever used by this population. Cocaine users had a more extensive drug abuse history, both legal and illicit.	Students who had used cocaine at some point during their lifetime scored higher on the EPQ P scale.
Bobes et al. (2002)	3,634 conscripts entering compulsory military service in Asturias (Northern Spain). The prevalences of lifetime, previous year and previous month 3,4-methylenedioxymethamphetamine (MDMA) use were 11%, 8% and 5%, respectively. MDMA ranked fifth among illicit drugs ever used.	Conscripts who had used MDMA during the year prior to study scored higher on the EPQ-A N and P scales.
King et al. (1995)	58 inpatient male alcoholics and 33 non-alcoholic controls. Alcoholics had higher levels of estradiol and total testosterone than controls.	Alcoholics scored higher than controls on the EPQ N and P scales.
Rosenthal et al. (1990)	202 male and 95 female substance users at a public-sector hospital facility (Memphis).	The users scored higher than nonusers on the EPQ P and N scales, and lower on the E scale. Alcohol, cocaine, opioid, and polysubstance users scored higher on all EPQ scales. Cocaine users scored relatively highest on the P scale, while polysubstance users scored highest on the E scale. The alcohol users scored highest on the N and L scales. Scores on the EPQ N scale were higher for both male and female alcoholics than for their normal-drinking co-twins.
Mullan et al. (1986)	54 twin-pairs.	Indian alcoholics scored higher than Caucasians on the EPQ P scale. AA members scored higher than non-members on the E scale and lower on the P scale.
Hurlburt et al. (1984)	91 American active members of Alcoholics Anonymous (AA) (at least six months of abstinence) were matched by race and sex with 91 alcoholics who had recently completed alcoholism treatment (non-AA members).	

*Notes:* The studies were identified by conducting thorough searches (31 August 2005) in Medline only, using combinations of the term "substance abuse" with the term "Eysenck Personality Questionnaire". E = extraversion; P = psychoticism; N = neuroticism; L = lie.

Table 3

*Studies on the predictive and discriminant validity of the Zuckerman sensation-seeking scales (SSS) with respect to substance abuse*

Study	Participants	Main findings
Gonzales et al. (2005)	109 American HIV+ and 154 HIV- polysubstance users with a history of dependence primarily for cocaine or cocaine/heroin.	Greater sensation seeking was associated with more risky sexual practices among HIV+ drug users.
Patkar et al. (2004)	141 African-American cocaine-dependent patients entering a 12-week intensive outpatient treatment program, and 60 controls.	Cocaine patients had higher scores than controls on total SSS. The SSS scores showed a negative correlation with days in treatment and negative urine samples, and a positive correlation with the dropout rate.
Gerra et al. (2004)	See Table 2 for a description of the participants.	Higher scores on total SSS and poor school achievement were associated with illicit drug use and “alcohol abuse” (multiple drug users).
Patkar et al. (2003)	105 African-American cocaine-dependent outpatients and 44 African-American controls.	Cocaine-dependent patients scored higher than controls on total SSS and on the Dis and TAS scales.
De et al. (2003)	80 men seeking treatment at an addiction clinic in India.	The early onset cluster of abusers (mean age at onset 21 years) had higher scores than late onset abusers (mean age at onset 27 years) on total SSS. They had also a higher lifetime use of sedatives and were more unemployed.
Limosin et al. (2003)	72 French alcohol-dependent male and female patients.	An association between a modification of sensitivity to dopamine in postsynaptic receptors (the DRD1 Ddel polymorphism) and SSS was found only in alcohol-dependent men.
Bayle et al. (2003)	11 French patients with kleptomania, 60 patients with alcohol use disorders, and 29 psychiatric patients.	Patients with kleptomania had higher scores than alcoholics and other psychiatric patients on total SSS and on the Dis scale.
Saiz et al. (2003)	See Table 2 for a description of the participants.	Students who had used cocaine at some point during their lifetime scored higher on total SSS.
Franques et al. (2003)	34 French opioid dependent participants, 34 participants from a paragliding club, and 34 controls (college staff), all matched for age and sex.	Opioid addicts and paragliders scored higher than controls on the SSS Dis and TAS scales. Paragliders scored higher than controls on the BS scale.
Martin et al. (2002)	77 American early and middle adolescent males and females recruited from a psychiatric clinic and 131 adolescents from two general pediatric clinics.	SSS was higher in males and females who reported nicotine and alcohol use and in males who reported marijuana use.
West (2002)	100 American previously substance-impaired and 100 nonimpaired registered nurses.	Scores on total SSS were higher in substance-impaired than nonimpaired nurses.
Bobes et al. (2002)	See Table 2 for a description of the participants.	Conscripts who had used MDMA during the year prior to study scored higher on total SSS.

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Laqueille et al. (2001)	73 French opiate drug addicts treated for 3 months with bupronorphine; 48 patients responded (still in the study at 3 months and absence of opiates in 75% of urinary samples).	Responders had lower scores than nonresponders on the SSS Dis scale.
Matsushita et al. (2001)	697 Japanese alcoholics and 270 controls. The study focused on a functional biallelic repetitive element in the 5' regulatory region of the serotonin transporter gene (5-HTTLPR).	The frequency of the homozygous short allele was higher in alcoholic binge drinkers than in nonbinge drinkers. There were no significant differences in the frequencies of either the 5-HTTLPR genotype or the short vs. long allele in alcoholic and control participants. No differences were found in SSS subscale scores between alcoholics with different 5-HTTLPR genotypes.
Dervaux et al. (2001)	100 French patients with schizophrenia or schizoaffective disorder (DSM-III-R); 41 of them were substance abusers.	Substance abusers had higher scores than nonabusers on total SSS.
Wagner (2001)	155 American undergraduate students.	SSS and anxiety sensitivity were predictors for substance abuse. A positive relationship between SSS and risky sexual behaviour was found. Participants with high scores on total SSS were most likely to engage in reckless driving, with male incidence being greater than female incidence.
Johnson & Cropsey (2000)	172 female and 84 male American college students.	Higher scores on total SSS predicted greater frequency of playing "drinking games", even after controlling for overall quantity and frequency of alcohol consumption. SSS was also related to specific motives for play. Men who scored high on SSS experienced more negative alcohol-related consequences as a result of play. In women, but not in men, heavy-drinking players had higher scores on SSS than heavy-nondrinking players.
Liraud & Verdoux (2000)	103 French inpatients; 45 had nonaffective psychotic disorders and 58 had mood disorders; 25% had a lifetime history of alcohol use disorder and 23% had a lifetime history of cannabis use disorder.	Those with alcohol use disorders scored higher on the SSS ES and Dis scales. Those with cannabis use disorder scored higher on the Dis scale.
Sarramon et al. (1999)	65 French patients admitted to a psychiatric ward, with or without addictive behaviours. The most frequent types of addiction were alcoholism and drug abuse.	Patients with one or several addictive behaviours had higher average scores on SSS. Each unit rise in the subscores of the SSS BS, Dis and TAS increased the risk of presenting with an addictive behaviour by a factor of 1.4 for the first two scales and by 1.3 for the third scale.
Marra et al. (1998)	44 French alcoholics.	Type 2 alcoholics (Cloninger's classification) scored higher on the TAS scale. The TAS scale differentiated abstinent alcoholics from these who relapsed.

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Duaux et al. (1998)	54 French opiate addicts and 70 controls. A subgroup (70%) scored high on SSS (raw score exceeding 24). There were no marked differences in genotype between opiate addicts and controls (the dopamine D3 receptor, DRD3, gene, assumed to be a candidate for drug dependence, was measured).	Opiate addicts scored higher than controls. Opiate addicts who scored above an SSS score of 24 were more frequently homozygotes for both alleles than patients with a score under 24 or controls.
Cernovsky et al. (1997)	119 Canadian addicts within an addiction treatment program.	These with higher scores on the SSS BS scale reported less satisfaction, whereas those with higher scores on TAS scale reported higher levels of treatment satisfaction.
Scourfield et al. (1996)	262 American addicts and 261 of their relatives with DSM-III-R diagnoses of drug and alcohol abuse and/or anxiety disorders.	Female participants with both substance abuse disorders and comorbid anxiety disorders had lower SSS TAS scores than those with substance abuse alone.
O'Connor et al. (1996)	125 American recovering drug users with three month abstinence from drugs. Drug users were divided according to drug preference: opiates, stimulants, marijuana, alcohol, and polydrugs.	Opiate users scored higher on the SSS BS scale than other users. Alcohol abusers scored higher on the SSS BS scale than stimulant, opiate and polydrug users.
Kaliski & Zabow (1995)	49 South African schizophrenic patients. No pattern of abuse differentiated the groups.	Schizophrenic patients with negative histories of violence scored higher than those with no history of violence on the SSS TAS scale.
Varma et al. (1994)	51 patients for alcohol dependence (DSM-II-R) attending a drug de-addiction clinic at a general hospital in India	Early onset alcoholics (age at onset of alcohol dependence 25 years or less) scored higher than the late-onset alcoholics on total SSS.
Pedersen et al. (1989)	1,027 Norwegian senior high school students aged from 16 to 19 years in the greater Oslo area.	The SSS subscale scores were moderately to strongly associated with the abuse of some drugs.
Allcock & Grace (1988)	10 New Zealand pathological gamblers, 10 alcoholics, 10 heroin addicts, and 25 nonpatients.	Drug addicts scored higher and alcoholics scored lower than pathological gamblers and the nonpatient group on total SSS. Drug addicts scored higher than the other groups on the SSS BS.
von Knorring et al. (1987)	1,129 18-years-old males called to the Enlistment Centre in the Northern part of Sweden; 96 had mixed drug abuse and 33 had pure alcohol abuse.	Drug abusers with a mixed pattern of abuse scored high on the SSS BS and TAS scales. They also had a low MAO activity.
Jaffe & Archer (1987)	125 female and 61 male American university undergraduate students; 24% had frequent use of alcohol and 15% had frequent use of marijuana. A high proportion of them tried (and/or used) other drugs, such as amphetamines (40%), cocaine (28%), tranquillisers (24%), barbiturates (18%), LSD (16%), other hallucinogens (13%, and solvents (10%).	Total SSS was the most powerful predictor of substance use and abuse among the five measures used (MMPI Pd, the MacAndrew alcoholism scale, the SSS, the Alcohol Abuse scale, and the Drug Abuse scale).
Khavari & Mabry (1985)	298 adult male and female members of labour unions.	High scores on the SSS Dis scale predicted psychosedative use.

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Galizio et al. (1985)	74 American male and female alcoholics (61 involved in a 30-day residential treatment program; 13 detoxified inpatients); subdivided into high ( $n = 28$ ) and low ( $n = 26$ ) sensation seekers, high sensation seekers were younger.	High sensation seekers had very high prevalence of marijuana use, and used stimulants, hallucinogens, sedatives (barbiturates and methaqualone), opiates (heroin and opiate pain killers), and tranquilisers regularly. The low sensation seekers used only tranquilisers (legally prescribed benzodiazepines).
Satinder & Black (1984)	48 male and female American college and university students.	Cannabis users scored higher than non-cannabis users on all of the four SSS scales. Total SSS and the SSS Dis scale remained significantly different when analysis of covariance, controlling for the use of alcohol, cigarettes, and LSD, was applied.
Galizio & Stein (1983)	121 male outpatients (chronic drug users) between the ages of 21 and 40 at three different drug programs in North Carolina. Two groups were created, polydrug and depressant drug users. The depressant group included participants who were daily users of heroin or other opiate or depressant drugs ( $n = 38$ ).	Polydrug users scored higher than depressant drug users on the total SSS scale and on the SSS TAS and ES scales.

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*Notes:* The studies were identified by conducting thorough searches (31 August 2005) in Medline only, using combinations of the term “substance abuse” with the term “sensation seeking scales”. Subscales from the SSS: BS = boredom susceptibility; Dis = disinhibition; ES = experience seeking; and TAS = thrill seeking and adventure seeking. Results from studies regarding tobacco users, and from studies included in the present thesis, are not presented in the table.

Table 4

*Studies on the predictive and discriminant validity of the Karolinska Scales of Personality (KSP) with respect to substance abuse*

Study	Participants	Main findings
Östlund et al. (2004)	316 females from a study "Women and alcohol in Göteborg"	Participants with DSM-III-R diagnoses of alcohol dependence and abuse scored higher on the KSP anxiety, impulsiveness, and irritability-related scales, and lower on conformity-related scales.
Stenbacka et al. (2004)	174 methadone patients (121 males and 53 females) and 387 untreated controls (191 men and 196 women) in Sweden.	Male patients had higher scores than male controls on the KSP SA, MT, I, Pt scales, and lower on the KSP So scale. Female patients differed most markedly on the KSP So scale; with patients' scores being lower. Later expulsion from treatment was predicted by low scores in the KSP So, SD, De, G, and S scales.
Hallman et al. (2001)	16 females with DSM-IV alcohol dependence, and 11 females with DSM-IV alcohol dependence and misuse of other drugs; all before the study, treated in Swedish hospitals for alcohol detoxication. The controls ( $n = 11$ ) female laboratory staff members.	Alcoholics with additional drug misuse had higher scores than those with alcohol dependence in the KSP I, SA, MT, PA, Pt, Irr, S scales, and lower scores in the KSP So scale. Alcoholics with additional drug misuse had lower platelet MAO activity than controls.
Nielsen et al. (1998)	804 Finnish alcoholic offenders, and controls (369 sibling pairs).	Tryptophan hydroxylase (TPH – the rate-limiting enzyme in the synthesis of serotonin) genotype, the intron 7 variant in the TPH gene, showed evidence for linkage to the KSP So scale.
Stålenheim et al. (1998)	61 nonpsychotic male offenders undergoing a forensic psychiatric evaluation at the Swedish Department of Forensic Psychiatry (in Uppsala); 36 had substance use disorder (DSM-III-R).	Total testosterone was associated with the KSP PA, S, and Inh scale. Free testosterone (FT-DPC) was associated with the KSP I, MA, So, and Irr scales.
Tönne et al. (1998)	32 Swedish patients in the treatment program for hypnotic/sedative (benzodiazepines, or a mixture of other hypnotic/sedatives including alcohol and/or analgesic) use disorder (DSM-III); 20 out of the 32 participants used benzodiazepines only (oxazepam, 11, diazepam, 3 lorazepam, 4 nitrazepam, and 3 flunitrazepam), and 12 of them had mixed substance use disorder; 19 out of the 20 benzodiazepine users had treatment success, compared to 7 out of the 12 participants with the mixed use substance disorder.	Those participants who had successful treatment outcome had lower scores than those who did not have successful treatment outcome in the KSP De, SA, MT, PA, S, G, Irr scales, and higher scores in the So scale.
Galligani et al. (1996)	Swedish groups of athletes in strength-based sports; 14 current anabolic androgenic steroid (AAS) users, 14 previous AAS users, and 14 nonusers.	Current users scored higher than previous users and nonusers on the KSP VA, MT, SD, I, IA scales.

Virkkunen et al. (1994)	58 Finnish alcoholics: violent offenders and impulsive fire setters (23 of them had antisocial personality disorder, 20 intermittent explosive disorder, and 15 were nonimpulsive offenders), and 21 healthy controls.	Alcoholics with antisocial personality disorder, intermittent explosive disorder and nonimpulsive offenders had higher scores than controls on the KSP PA, SA, and MT scales. Those with antisocial personality disorder and intermittent explosive disorder had higher scores than controls on the KSP De, IA, and S scales. Those with antisocial personality disorder had higher scores than those with intermittent explosive disorder on the KSP MA scale. The concentration of 5-HIAA in CSF was positively associated with the KSP InhA scale. Testosterone concentration in CSF was negatively associated with the KSP So scale.
Mukasa et al. (1990)	16 methamphetamine dependents, 10 alcohol dependents (all male inpatients at Kaisei Hospital, Japan), and 13 controls.	Dependents had higher scores than controls on the KSP I scale. Alcohol dependents had lower scores and methamphetamine dependents had higher scores than controls on the KSP VA scale. Methamphetamine dependents had lower scores than controls on the KSP Inh scale.
Hallman et al. (1990)	Female Swedish alcoholics subdivided into two groups, type I and type II alcoholics. (Type II is one with early onset and high genetic predisposition with a high degree of depression and alcoholism in first degree relatives, with a mixed drug abuse and social complications, and low platelet MAO activity).	In contrast to type II male alcoholics, the female type II alcoholics did not differ on any KSP scale.
L. von Knorring, A. L. von Knorring et al. (1987)	Male Swedish alcoholics subdivided into two groups, type I and type II alcoholics, and controls.	Type II alcoholics had higher scores than type I alcoholics on the KSP SA and VA scales, and lower scores on the So scale. Type II differed from both type I and controls on the I, MA, and So scales.
von Knorring et al. (1987)	1,129 18-year-old males called to the Enlistment Centre in the Northern part of Sweden; 96 had mixed drug abuse and 33 had pure alcohol abuse.	Both groups of drug abusers with mixed pattern of abuse and pure alcohol abuse scored higher than other 18-year-olds on the KSP I and MA scales.
Rydellius (1983)	50 Swedish "high alcohol-consumers" and 50 "0-consumers" selected from a sample of 862 18-year-old males	High alcohol-consumers had "psychopathic" personality traits, while 0-consumers had normal personalities

*Notes:* The studies, with one exception, were identified by conducting thorough searches (30 August 2005) in Medline only, using combinations of the term "substance abuse" with the term "Karolinska Scales of Personality". The exception is the study of Tönne et al. (1998), which was not listed on Medline, but it was known to the author and included in the table, because it was relevant to the topic of this thesis. I = impulsiveness; M = monotony avoidance; So = socialisation; SA = somatic anxiety; MT = muscular tension; PA = psychic anxiety; Pt = psychasthenia; IA = indirect aggression; VA = verbal aggression; Irr = irritability; S = suspicion; G = guilt; SD = social desirability; De = detachment; Inh = inhibition of aggression. Results from studies regarding tobacco users, and from studies included in the present thesis, are not presented in the table.

## **Theory and measurement of psychopathy**

### *Cleckley's classical theory*

Harvey Cleckley (1941/1988) described psychopathy in his classical book *The Mask of Sanity*. He outlined 16 criteria for psychopathy, but these criteria were not sufficiently defined to enable interrater reliability to be determined, and these criteria, therefore, were considered to be rather vague and subjective (Hare, 1980). Two Swedish researchers and forensic psychiatrists (Sten Levander and Lars Lidberg) classified offenders along a 7-point scale of psychopathy in experimental studies of the association between several physiological correlates and psychopathy. They based their work on Cleckley's theory, and on the measurement of personality traits based on Sjöbring's and Eysenck's theories (for several empirical studies see Levander, 1976).

### *The current theory and measurement of psychopathy*

Rating of psychopathy in offenders has a long tradition. Hare (1991, 2003) developed a method based on a checklist known as the "Psychopathy Checklist-Revised (PCL-R)", for identifying offenders with psychopathy. The PCL-R measures interpersonal and affective personality traits and socially deviant behaviour (see the *Methods*).

The PCL-R is now standard for rating this syndrome in forensic and correctional settings (Fulero, 1995; Stone, 1995). Psychopathy has traditionally been conceptualized and the concept has been applied for adult offenders. Influential researchers on this topic (e.g., Robins, 1978) have, however, postulated that psychopathic traits may be observed very early, as early as 6-10 years of age. Consequently, several studies have shown that psychopathy may be validly and reliably rated in children (e.g., Frick, O'Brien, Wootton, & McBurnett, 1994) and in young offenders (e.g., Spain, Douglas, Poythress, & Epstein, 2004). Psychopathy Checklist: Youth Version (PCL:YV) (Forth, Kosson, & Hare, 2003), may be used to rate psychopathy in children and adolescents. Published studies have applied three different versions of the PCL:YV, predominantly in samples of juvenile delinquents. The first version (Forth, Hart, & Hare, 1990) has been referred to as a "modified PCL-R" (e.g., Frick et al., 1994), the second version (Forth, unpublished report) has often been referred to as a PCL:YV "research version" (e.g., Corrado, Vincent, Hart, & Cohen, 2004), while the third version is the above-mentioned (still in press) version (Forth et al., 2003).

### *Predictive and discriminant validity of the four facets of the PCL-R, with a focus on substance abuse*

A search on Medline for "PCL-R and substance abuse" resulted in a list of 23 publications. An analysis of the results reported in these publications showed that the PCL-R has good discriminant validity in the population of people with substance use disorder. No studies, however, discussed the validity of the 2-factor 4-facet model (for details see the *Methods*) of the PCL-R.

## **Aims of the present thesis**

One aim of this thesis was to evaluate the prevalence of FZ abuse in two Swedish populations of violent offenders, to describe these offenders and to study their personalities in a quantitative manner. The members of these two populations had a polysubstance abuse pattern, but we believed that many of them would be FZ abusers.

Specifically, the aims of the studies included in the thesis were to answer the following questions:

- How prevalent is FZ abuse in male juvenile delinquents in correctional institutions and in male offenders referred to an FPE in Sweden?
- Why do FZ abusers abuse just FZ (and not another substance)?
- Do their traits, behaviour or other psychiatric or psychological characteristics change while intoxicated with FZ?
- Are there subjective differences between FZ and other benzodiazepines?
- How do FZ abusers obtain FZ?
- Are the background factors and descriptive characteristics of FZ abusers different from those of non-FZ abusers?
- Are the crimes of FZ abusers different from those of non-FZ abusers?
- Is FZ abuse reflected in psychiatric diagnoses?
- Are there associations between FZ abuse and any specific kind of crime?
- Are certain personality traits of FZ abusers (e.g., impulsiveness, aggressiveness, sensation seeking, psychoticism, anxiety, socialization), different from those of non-FZ abusers?
- Are there associations between FZ abuse and psychopathic traits and lifestyle?
- Is it possible to use case descriptions to illuminate some legal issues relating to FZ and its position on the market?

## **METHODS**

### **Participants and settings**

Participants in the studies described in the present thesis were nonpsychotic male offenders: a sample of offenders undergoing a forensic psychiatric evaluation (FPE); and a sample of juvenile delinquents. Table 5 shows the relevant characteristics of the participants, and a comparison between the two samples of participants.

#### *Offenders referred for a forensic psychiatric evaluation (Studies II-IV)*

The potential sample of male offenders comprised those who were not older than 35 years and who underwent an FPE at the Department of Forensic Psychiatry in Stockholm between November 1997 and November 1998. This amounted to 94 potential subjects. Criteria for exclusion were the need for an interpreter (14 subjects), and the withholding by the forensic psychiatric team of permission to participate because of obvious psychotic disorder or mental retardation (five subjects). Medication was not a reason for exclusion. Six subjects could not be assessed for administrative reasons, one subject committed suicide, eight

subjects refused to participate in the assessments, although all of these subjects did give permission for their files to be studied (two of them were interviewed regarding their FZ abuse by other clinicians and their files were studied by me; the results from these two cases are included in Study III). This left 60 participants (the “forensic psychiatric sample”) to be assessed with respect to psychopathy, personality traits, and information about substance use disorders in general, and FZ abuse in particular. (Several participants did not fill in self-reported personality inventories, see Study II, Table 3, Note 3).

The intellectual capacity of the participants was estimated either by the Wechsler Adult Intelligence Scale-Revised (WAIS-R) (Wechsler, 1981) or by a Swedish standard intelligence battery (SRB) developed by Dureman and Sälde (1959). All participants satisfied the inclusion criterion that they have an IQ that the forensic psychiatric team considered to be “normal”. (It was decided that subjects with mental retardation should not participate in the project (see below), because this project concerns learning disorders, particularly reading disorder (“dyslexia”) and disorder of written expression. DSM-IV (American Psychiatric Association, 1994) allows, however, a diagnosis of learning disorder that is independent of the diagnosis of mental retardation, and therefore, it was decided that these subjects who had a diagnosis of a mild retardation, could participate in the project. Two participants<sup>7</sup> had a mild mental retardation, which means an IQ level between 50-55 to approximately 70.)

Diagnoses of mental disorders (DSM-IV) were confirmed during the FPE (see Trygg, 2000, for a description of psychiatric diagnoses, comorbidities among them, and psychological methods used during the participants’ FPEs, and see Studies II and III for descriptions of the psychiatric diagnoses in FZ abusers).

Forty-four participants had a diagnosis on Axis I (clinical disorders and other conditions that may be a focus of clinical attention); 20 had substance use disorders (alcohol-related disorders ( $n = 10$ ), polysubstance dependence ( $n = 4$ ), cannabis abuse ( $n = 3$ ), amphetamine abuse ( $n = 1$ ), opioid dependence ( $n = 1$ ), sedative, hypnotic, or anxiolytic dependence ( $n = 1$ )), mood disorders ( $n = 9$ ), eight had schizophrenia and other psychotic disorders, four had cognitive/neuropsychiatric disorders (such as ADHD, Asperger’s syndrome), two had anxiety disorders, and one had partner-relational problems<sup>8</sup>; all of them stated as the first diagnosis on Axis I. Those who had any diagnosis on Axis I had on average 2 diagnoses ( $SD = 1.20$  diagnoses; range 1-6 diagnoses).

Forty-two participants had a diagnosis on Axis II (personality disorders and mental retardation); 39 of them had some form of personality disorder (personality disorder not otherwise specified ( $n = 13$ ), antisocial personality disorder ( $n = 11$ ), borderline personality disorder ( $n = 9$ ), paranoid personality disorder ( $n = 2$ ), narcissistic personality disorder ( $n = 2$ ), schizotypal personality disorder ( $n = 1$ ), dependent personality disorder ( $n = 1$ ), stated as the first diagnosis on Axis II. In addition, two participants had a diagnosis of mild mental retardation (“borderline intellectual functioning”) and one participant had a diagnosis of “hyperactivity”, stated as the first diagnosis on Axis II. Those who had any diagnosis on Axis II had on average 1.5 diagnoses ( $SD = 0.62$  diagnoses; range 1-3 diagnoses).

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<sup>7</sup> Both participants had dyslexia, which was first diagnosed in the present project; they showed a markedly discrepancy between verbal and nonverbal IQ with at least normal level of the nonverbal IQ.

<sup>8</sup> According to DSM-IV (American Psychiatric Association, 1994): “In practice, most psychosocial and environmental problems will be indicated on Axis IV. However, when a psychosocial or environmental problem is the primary focus of clinical attention, it should also be recorded on Axis I” (p. 29).

This thesis deals with “mentally disordered” male offenders, as its title states, and it is interesting to note how many participants had no diagnosis at all on the two main axes of the DSM-IV. Out of the 18 participants who had no diagnosis on Axis I, five of them did not have any diagnosis on Axis II.

There were only a few diagnoses indicated on Axis III (general medical conditions, which are coded with the *International classification of diseases, 10th Revision, Clinical modification* (ICD-10CM, World Health Organization, 1992) codes); only 10 out of the 60 participants had such diagnoses and the most frequent ( $n = 3$ ) among these was hepatitis.

Axis IV is for reporting psychosocial and environmental problems, which, according to DSM-IV “may affect the diagnoses, treatment, and prognosis of mental disorders (Axes I and II)” (p. 29). Fifty-six out of the 60 participants had received a diagnosis of one or more problems on this axis. The most relevant problems (mentioned first on this axis), as they were labelled in the participants’ forensic files, and their frequencies (grouped here according to the classification proposed by DSM-IV (p. 29)) were as follows: (a) problems with primary support group such as “conflicts within a primary group” ( $n = 18$ ), “divorce or separation” ( $n = 8$ ), “problem with nuclear family” ( $n = 2$ ), “abuse in a family member ( $n = 2$ ), or “a disease in a relative ( $n = 1$ ); (b) problems related to the social environment, such as “deficiency or problem with the social network” ( $n = 10$ ), “death of a relative” ( $n = 3$ ), “problems with relationships” ( $n = 2$ ), or “general difficulties in adapting oneself” ( $n = 1$ ); (c) housing problems such as “homelessness” ( $n = 2$ ); (d) problems related to interaction with the legal system/crime such as “own criminality” ( $n = 2$ ); (e) other psychosocial and environmental problems such as “discord with social worker” ( $n = 3$ ), “own accident” ( $n = 1$ ), or “an unsuccessful substance abuse treatment” ( $n = 1$ ).

A clinician usually reports his or her judgment of the evaluated person’s overall level of psychological, social and occupational (and not physical functioning or environmental limitations) functioning on Axis V. According to DSM-IV, this information may be used in the planning of treatment, its impact, and in predicting its outcome. A global assessment of functioning (GAF) scale is used to report the level of functioning (see DSM-IV, pp. 30-32); it ranges from a value of 100 (superior) to 0 (no information). The mean GAF scale concerning the highest level of overall level of functioning during the past year was 55.1 ( $SD = 15.1$ , range 21-90), and at the time of the FPE it was 53.3 ( $SD = 15.7$ , range 11-80). This level of functioning (i.e., a GAF value between 51 and 60) indicates “moderate symptoms (e.g., flat affect and circumstantial speech, occasional panic attacks) or moderate difficulty in social, occupational, or school functioning (e.g., few friends, conflicts with peers or co-workers” (American Psychiatric Association, 1994, p. 32).

The FPE did not focus on all of the mental disorders according to DSM-IV (e.g., reading disorder, disorder of written expression, attention-deficit hyperactivity disorder, substance use disorders of specific substances), and we therefore attempted to describe the prevalence of some of these disorders during the projects.

The personalities and mental health of the participants have been studied since 1997 within a research project on neuropsychological functions: “Dyslexia in young males who are referred to a forensic psychiatric evaluation: Psychological, social, and biological characteristics”. Studies carried out within this project have focused on the prevalence of reading disorders and/or disorders of reading expression (dyslexia) (Dåderman & Lidberg, 2005; Selenius, 2002; Selenius, Dåderman, Wirsén Meurling, & Levander, 2005), on the relationship between dyslexia and neuropsychological functions (Dåderman, Selenius,

Wirsén Meurling, & Levander, 2005), on FZ abuse (Studies II-IV; Dåderman, 2000; Dåderman, Strindlund, Wiklund, Fredriksen, & Lidberg, 2003), on psychopathy (Study IV; Dåderman, 2005), on personality traits (Study II; Elving, 2003), on the alcohol habits and alcohol-related symptoms (Wennberg & Dåderman, 1999, 2000), on the psychiatric diagnoses and psychological tests (Trygg, 2000; Trygg et al., 2001; Wiklund et al., 2002), on the retrospective ratings of childhood ADHD symptoms (Dåderman, & Kristiansson, 2005; Klint, 2001; Selenius & Dåderman, 2004), and on the relationship between self-esteem and birth-order (Fyring, 2001; Malgir, 2003, 2004).

### *Juvenile delinquents (Studies I and IV)*

The potential sample consisted of 63 adolescent male juvenile delinquents from four Swedish national correctional institutions. Three of these juveniles refused to participate, while a further four were prevented from entering the study by objections from the staff (one because the IQ of the juvenile was below 70, one was “too dangerous”, one because “we have poked our nose quite enough into his life”, and one was “too frail”). This left 56 participants (the “juvenile sample”) to be assessed with respect to psychopathy, personality traits (one participant did not fill in personality scales), and substance use disorders with a focus on FZ abuse. The institutions that provided care for the present sample consisted of six closed-emergency departments (maximum security), two closed-correctional departments, and four open-correctional departments. The average length of stay at the current institution, up to the date of the assessment in 1996, was 12 weeks ( $SD = 15.8$ ; range 1-52 weeks). In most cases, it was not known at the time of the study how long the participant would remain committed to an institution.

All participants fulfilled the DSM-IV criteria for conduct disorder, implying criminal activity, drug abuse, etc., before the age of 15 years. All participants with immigrant backgrounds spoke adequate Swedish. The majority of those with immigrant backgrounds were brought up in Sweden, and all had undergone compulsory schooling in Sweden. Information in the files showed that the participants came predominantly from lower class and middle class families.

The personalities and mental health of one group of 47 juvenile delinquents have been studied since 1996 in a project: “Dr Jekyll and Mr Hyde – behaviour patterns among young male delinquents with a combined abuse of alcohol and benzodiazepines: Biological and psychological indicators” (Study I; Dåderman, 1996; Dåderman, 1999; Dåderman, Wirsén Meurling, & Hallman, 2001). The personalities and mental health of another group of a further nine participants from a special security department for severe male juvenile delinquents have also been studied since 1997 in a project: “Reading disabilities in severe conduct-disordered juvenile delinquents – psychological, social, and biological indicators” (Dåderman et al., 2005; Selenius, 2003; Selenius & Dåderman, 2004). Data from these two groups of juvenile delinquents were merged into one sample for the study reported here into the personality traits and psychopathy of the participants, and on the psychometric values of the instruments used (Dåderman, 2002b; Dåderman, Hellström, Wennberg, & Törestad, 2005; Dåderman & Kristiansson, 2003, 2004). Two additional studies used data from the pooled sample (see Table 5); these studies focused on the relationship between psychopathic traits and lifestyle in the FZ abusers (Study IV), and on memory performance in the dyslexic juvenile delinquents (Selenius, Dåderman, & Hellström, 2005).

Table 5

*Sample characteristics*

Characteristic	Pooled total sample	Forensic sample	Juvenile sample	<i>p</i> <sup>1</sup>
	<i>N</i> = 114	Mean $\pm$ (range) <i>n</i> = 60	<i>n</i> = 54 <sup>2</sup>	
Age <sup>3</sup> , years	22.5 $\pm$ 6.6 (14-35)	27.4 $\pm$ 5.5 (16-35)	17.1 $\pm$ 1.2 (14-20)	< .00045
Education <sup>4</sup> , years	9.2 $\pm$ 1.9 (3-14)	10.1 $\pm$ 1.8 (5-14)	8.3 $\pm$ 1.5 (3-11.5)	< .00045
<i>Psychopathy measures</i>				
Total PCL-R score	26.0 $\pm$ 8.8 (2.1-40)	23.0 $\pm$ 8.6 (2.1-37.9)	29.2 $\pm$ 7.8 (11.8-40)	< .00045
Factor 1 (Interpersonal/Affective)	9.8 $\pm$ 3.9 (1-16)	9.0 $\pm$ 3.9 (1-15.5)	10.7 $\pm$ 3.8 (1-16)	.019
Facet 1 (Interpersonal)	4.0 $\pm$ 2.3 (0-8)	3.4 $\pm$ 2.2 (0-8)	4.8 $\pm$ 2.2 (0-8)	.0001
Facet 2 (Affective)	5.9 $\pm$ 2.1 (1-13)	5.7 $\pm$ 2.1 (1-8)	6.1 $\pm$ 2.1 (1-13)	.318
Factor 2 (Social deviance)	13.1 $\pm$ 4.0 (0.6-18)	12.1 $\pm$ 4.3 (0.6-18)	14.3 $\pm$ 3.4 (5.6-18)	.003
Facet 3 (Lifestyle)	7.5 $\pm$ 2.4 (0.5-10)	7.0 $\pm$ 2.6 (0.5-10)	8.1 $\pm$ 2.0 (2.6-10)	.012
Facet 4 (Antisocial)	6.8 $\pm$ 2.6 (0.1-10)	6.0 $\pm$ 2.7 (0.1-10)	7.7 $\pm$ 2.1 (2.7-10)	< .00045
<i>Theoretically relevant<sup>5</sup> psychopathy-related personality traits (KSP)<sup>6</sup></i>				
	<i>N</i> = 100	<i>n</i> = 47	<i>n</i> = 53	
Impulsiveness	66.4 $\pm$ 15.2 (31.8-102.2)	65.6 $\pm$ 15.2 (38.6-102.2)	67.1 $\pm$ 15.4 (31.8-101.5)	.631
Monotony avoidance	61.1 $\pm$ 13.8 (28.7-87.8)	55.1 $\pm$ 14.5 (28.7-87.8)	66.5 $\pm$ 10.5 (39.5-87.8)	< .00045
Socialisation	22.0 $\pm$ 12.9 (-5.1-51.5)	21.2 $\pm$ 13.1 (-2.6-49.8)	22.7 $\pm$ 12.9 (-5.1-51.5)	.557
Detachment	55.0 $\pm$ 11.4 (18.3-86.7)	53.8 $\pm$ 13.1 (18.3-86.7)	56.1 $\pm$ 9.7 (31.3-76.1)	.331
		No. (%) of participants		
Similarity score <sup>7</sup>	29 (25.4)	18 (30.0)	11 (20.4)	.238
<i>Ethnicity and family situation</i>				
At least one parent not born in	50 (43.9)	23 (38.3)	27 (50.0)	.210

Sweden <sup>8</sup>				
Heredity for substance abuse and/or for other mental disorder <sup>9</sup>	34 (29.8)	19 (31.7)	15 (27.8)	.650
Child and adolescent psychological or psychiatric contact	43 (37.7)	28 (46.7)	15 (27.8)	.038
<i>The five main substance use (DSM-IV)<sup>10</sup> disorders</i>				
Alcohol	57 (50.0)	24 (40.0)	33 (61.1)	.024
Cannabis or marijuana	48 (42.1)	21 (35.0)	27 (50.0)	.105
Flunitrazepam (e.g., Rohypnol)	39 (34.2)	18 (30.0)	21 (38.9)	.318
Amphetamines and/or cocaine	36 (31.6)	19 (31.7)	17 (31.5)	.983
Opiates (heroin)	19 (16.7)	6 (10.0)	13 (24.1)	.044
<i>Past and present<sup>11</sup> violent sentences</i>				
Violent offences	86 (75.4)	45 (75.0)	41 (75.9)	.909
Robbery <sup>12</sup>	26 (22.8)	14 (23.3)	12 (22.2)	.888

*Notes:* PCL-R = Psychopathy Checklist-Revised (Hare, 1991, 2003). KSP = Karolinska Scales of Personality (Gustavsson, 1997; Schalling, 1986; Schalling et al., 1987). <sup>1</sup>*p*-value for the differences between forensic and juvenile delinquent participants; two-tailed *t*-tests or Chi-squared tests were used. Some researches (e.g., Brace et al., 2003) prefer to report the value of “*p* < .0005” in the case of “*p* = .0000”, while others and me have chosen the value of “*p* < .00045”. The level of significance was not corrected for the risk of spurious significance. When employing the Bonferroni correction (Howell, 1997), statistical significance less than or equal to .002 remains significant. <sup>2</sup>Two of the members of this sample were also members of the forensic sample, and they have therefore been excluded from the second one. <sup>3</sup>At the time of the interviews and assessments of flunitrazepam abuse, that is, 1997-1998 for the forensic sample, and 1996 or 1998 for the juvenile sample. <sup>4</sup>A life-long education for the forensic sample is presented, that is, not only the education level from the school-age time, but also education obtained during adulthood. <sup>5</sup>See Schalling (1978). <sup>6</sup>The KSP scale scores are presented as age-adjusted and sex-adjusted T-scores with a mean of 50 (*SD* = 10) (Bergman et al., 1988); it is commonly accepted in clinical practice that psychological scale scores between T-scores of 40 and 60 are within a “normal range”. <sup>7</sup>The similarity score was scored “1” in the statistical file if a participant from the forensic sample had previously been assessed and treated at youth correctional institution as an adolescent, or a participant from the juvenile sample had ever been referred to a forensic psychiatric evaluation; the lack of these circumstances was scored “0”. <sup>8</sup>Alternatively, the subject was born of both non-Swedish parents and adopted by Swedish. <sup>9</sup>Father and/or mother addicted to alcohol or drugs, and/or diagnosed with major mental disorder (schizophrenia, manic-depressive psychosis, psychogenic psychosis or other psychosis), and therefore treated at a psychiatric clinic. <sup>10</sup>Only main types of current history of abuse/dependence disorders are presented. <sup>11</sup>All offences according to official records. <sup>12</sup>Robbery *per se* is not a violent crime according to Swedish law and is therefore presented separately.

## **Instruments**

### *Structured interviews (Studies I-IV)*

The structured face-to-face interview (Studies I and II) lasted approximately one and half hours and collected background information. The structured interview was extended for the forensic psychiatric sample with questions regarding alcohol habits (for the questions in English, see Wennberg & Dåderman, 1999, 2000) and regarding some issues related to dyslexia (for the questions in English, see the Appendix; Dåderman, Lindgren, & Lidberg, 2004).

FZ abuse in both samples was established using a structured interview based on the DSM-IV criteria. Thus, FZ abusers fulfilled the criteria for sedative, hypnotic, or anxiolytic abuse (305.40), generally referred to as “substance abuse”, by the DSM-IV (American Psychiatric Association, 1994, pp. 182-183) (for the questions used in the forensic sample, in Swedish and in English, see Appendix 2 and 3, respectively). This interview was based on the guidelines of the Swedish version of the Structured Clinical Interview for DSM-IV - Axis I Disorders (SCID-I), developed by First, Gibbon, Spitzer, Williams, & Benjamin (1997).

### *Unstructured interviews (Studies I and II)*

One aim of the studies described in this thesis was to answer the question: “Why do FZ abusers abuse just FZ (and not another substance)?” The best way to answer this question was to pose it to FZ abusers who had a broad experience of being often intoxicated with it. In order to conduct an in-depth study of the participants’ abuse of FZ, formal, unstructured interviews, based on the inter-personal communication theory (Banaka, 1971), were also used (Studies I-II). The questions were open-ended to encourage participants to describe experiences from their perspective. For example, one question was: “Why do you abuse FZ (and not another substance)?” Another question was: “What does it mean to be intoxicated with FZ?”

### *Grounded theory*

A “grounded theory” analysis was used (for details see the subsection *Qualitative analysis*). Grounded theory is a form of a qualitative inductive research approach, which is systematically generated from data (Glaser, 1978) by using constant comparison procedures (Glaser & Strauss, 1967) to discover the social- psychological processes inherent in a phenomenon (Strauss & Corbin, 1990). The resulting theory identifies patterns in the data and relationships between patterns.

### *Official files (Studies I-IV)*

Files from the Swedish National Board of Forensic Medicine were examined (Studies II-IV). These files included information from the Swedish National Police Register, the Hospital Discharge Register of the Swedish National Board of Health and Welfare, and documents from the courts. We have also studied autopsy material from the Swedish National Board of

Forensic Medicine, including photos and descriptions of the victims' injuries, and documents and videotapes from the criminal investigations that were carried out (Study III). The Swedish National Police Board supplied information regarding offences committed by the juvenile delinquent participants after they had reached the age of fifteen. This data covered all offences leading to public prosecution and conviction, and was obtained for all participants about 18 months after the interviews. We hoped that this information would supplement the interview data regarding previous criminal offences. Files from the correctional institutions were also studied.

### *Personality inventories (Studies I and II)*

The construction of personality inventories is based on the assumption that individual differences can be measured with a questionnaire. The following four personality inventories have been used to measure traits that are assumed to reflect the biological basis of personality.

#### *The Marke-Nyman Temperament (MNT) inventory (only Study II)*

The MNT is a Swedish personality inventory constructed by Marke and Nyman (Barett, 1972; Coppen, 1966; Nyman, 1956; Nyman & Marke, 1962), based on Sjöbring's personality theory (Sjöbring, 1958/1973, (see the *Introduction* for a description of the Sjöbring dimensions). The questionnaire consists of 60 true/false items. Three scales are included in the inventory: validity, stability, and solidity; each corresponding to 20 items of the questionnaire. Every item (as used in this thesis) is scored 1 ("Yes") or 0 ("No"), and a scale score is calculated as the sum of the item scores (for details, see the manual, Nyman & Marke, 1962, p. 21).

Nyman and Marke (1962) showed that the MNT scales are stable over time: the two month test-retest reliability<sup>9</sup> coefficients ranged from .78 to .89. Engström (1997) studied MNT in a sample of patients who had attempted suicide, and he showed good reliability of the MNT scales in terms of internal consistency, measured by Cronbach's alpha<sup>10</sup>. Cronbach's alpha in Engström's study was .86, .70, and .76 for the validity, stability, and solidity scales, respectively.

Engström (1997) has also examined the construct validity of the MNT by studying relationships between scales from the MNT, EPQ-I and KSP (see below). Low validity (*sub-validity*, i.e. being easily tired, having a low activity level, and having low self-esteem) was associated with different forms of anxiety and neuroticism. High solidity (*super-solidity*, i.e., being objective, unchangeable, and independent) was associated with high socialisation, high values in the social desirability scale, and low impulsiveness, indicating that high solidity reflects conformity and social adjustment as well as nonimpulsiveness. High stability (*super-stability*, i.e., being sophisticated, having a high level of abstraction, being skilful with emotional distance towards other people, and low empathy) was positively associated with detachment. In that study, all three MNT scales were positively associated

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<sup>9</sup> The test-retest reliability measures the stability of a scale and is often expressed as a reliability coefficient. This is simply the correlation coefficient (Pearson correlation coefficient,  $r$ ) between the scores obtained by the same persons on two administrations of the test (Anastasi, 1968).  $R$  ranges from -1 to 1. It is commonly accepted that a value of  $r$  of at least .30 is acceptable (Tabachnick & Fidell, 1996).

<sup>10</sup> Cronbach's alpha is a measure of reliability that ranges from 0 to 1, with values of .60 to .70 deemed the lower limit of acceptability (Nunnally, 1978).

with extraversion-related scales. Low solidity was associated with high impulsiveness in juvenile delinquents in the study of Schalling and Holmberg (1970). Impulsiveness is included in the concept of psychopathy used by Cleckley (Hare & Cox, 1978). We can conclude that the MNT scales show adequate construct validity.

### *The Eysenck Personality Questionnaire (EPQ)*

The version of the EPQ known as “EPQ-I” (Eysenck & Eysenck, 1975) was used in the work reported here. This version includes an impulsiveness scale from the Impulsiveness-Venturesomeness-Empathy (IVE) inventory (Eysenck & Eysenck, 1978). Schalling translated both the EPQ and IVE-I into Swedish in the 1970s, and this Swedish version of the EPQ, called EPQ-I, has been widely used in Sweden. The EPQ is a version of the series of brief inventories Hans J. Eysenck and Sybil B. G. Eysenck published as practical implementations of the basic orthogonal (i.e., uncorrelated) dimensions proposed by Eysenck in the 1950s. The initial questionnaire was the Maudsley Medical Questionnaire, which included only the neuroticism scale. The Maudsley Personality Inventory, a measure of both neuroticism and extraversion, followed. The Eysenck Personality Inventory (EPI) (Eysenck & Eysenck, 1964) succeeded the Maudsley Personality Inventory (and is still in use). The EPI measures neuroticism and extraversion, and it includes a lie scale to detect people who are “faking good”. The EPQ, which (in both adult and junior versions) measures the same dimensions as the EPI, was subsequently published (Eysenck & Eysenck, 1975) and formally introduced a psychoticism scale. An additional inventory, the Eysenck Personality Questionnaire (Revised), is also available, designed to measure four dimensions of personality (psychoticism or tough-mindedness, extraversion, neuroticism or emotionality, and addiction), and it includes a lie scale. The inventories have been described and reviewed in different editions of the *Mental Measurement Yearbook* (MMY), where many references can be found. Four reviewers first reviewed the EPQ in the eighth edition of the MMY, separately; Block, Kline, Stricker, and Tellgens. One of them (Block, 1978) concluded, that, “much more psychometric, conceptual, and validation work is required before the EPQ (or its successors) can be usefully employed by the scientific community” (p. 809).

The EPQ-I version consists of 114 true/false items, and the resulting inventory is classified into five scales: extraversion, neuroticism, psychoticism, a lie scale, and the impulsiveness scale. The number of items in the scales is 21, 23, 25, 21, and 24, respectively. Every item (as used in this thesis) is scored 1 (“Yes”) or 0 (“No”), and summed to a scale score. (Some items have a reversed scoring, and the use of 0 for “Yes” and 1 for “No” for these items, while at first sight illogical, is required for technical reasons).

Previous research on female and male samples from both the law-abiding and the criminal population has shown that the scales from the EPQ have good construct validity and reliability (for a review see Eysenck & Gudjonsson, 1989; for a review regarding the predictive and discriminant validity of the EPQ, focused on substance use disorders, see the *Introduction*). Engström (1997) established in the previously mentioned sample of patients who attempted suicide that all scales are reliable in terms of internal consistency, measured by Cronbach’s alpha (which ranged from .65 to .89). Landahl (2002) and Haapaniemi (2004) evaluated psychometric values of the EPQ-I in two different samples of college students. The results showed that reliability measures of all scales were satisfactory: Cronbach’s alpha ranged from .75 to .89 in Landahl’s study, and from .71 to .88 in Haapaniemi’s study.

### *The Zuckerman Sensation-Seeking Scales (SSS)*

The Zuckerman questionnaire used to measure the sensation-seeking trait has undergone a number of revisions since the introduction of the first version (Zuckerman, Kolin, Price, & Zoob, 1964). SSS-V (the “V” is the version number) (Zuckerman, 1994) consists of 40 forced-choice items (10 items for each scale). SSS measures four specific components of sensation-seeking behaviour, from which the following subscales are derived: thrill and adventure-seeking (TAS), experience-seeking (ES), disinhibition (Dis), and boredom-susceptibility (BS). The sum of the four subscales is expressed in a total score. Every item is scored 1 or 0, according to a scoring key proposed by Zuckerman (1979, 1994), and summed to give a scale score. Some items express a desire or an intention to engage in sensation-seeking activities, while other items report preferences for activities already experienced. The remaining items reflect general attitudes.

People who receive high scores on BS have an aversion to routine activities, work, and to boring people. People who receive high scores on TAS show a tendency to do things that are a little frightening, and these people have a desire to engage in physically risky activities or sports (such as parachuting, scuba diving, or downhill skiing) that provide unusual sensations of speed or the defiance of gravity. High scores on the ES scale indicate a tendency to seek novel sensations and experiences through the mind and senses. Typical examples are the sensations found when listening to arousing music, and through social nonconformity, such as association with groups on the fringes of conventional society. The reliability measured by a test-retest coefficient (3-week retest) is high, .94 (for a detailed review regarding psychometric measures of different versions of the SSS, see Zuckerman, 1979, 1994). The reliability of the SSS-V total scale in terms of the internal consistency for the normative sample (Zuckerman, 1979) ranges from .83 to .86. All subscales show good reliability.

The validity of SSS-V is well-established (e.g., Zuckerman, 1984, 1994), indicating that the scales are associated with engaging in a greater variety of heterosexual activities with more partners, drug use, volunteering for experiments and unusual activities (sensory deprivation, hypnosis, or drug studies), physically dangerous activities, and gambling (Zuckerman, 1980). See the *Introduction* for a review of the predictive and discriminant validity of the SSS-V, focused on substance use disorders.

### *The Karolinska Scales of Personality (KSP)*

Schalling and her co-workers studied several scales and separate items that had been previously published. They analysed the logical content of the scales and used factor analysis to develop new scales. These scales are called the Karolinska Scales of Personality (KSP) (Gustavsson, 1997; Schalling, 1986; Schalling et al., 1987). The KSP questionnaire consists of 135 items, grouped into 15 scales (for a description of the scales, see Schalling et al., 1987). The length of the scales ranges between 5 items (hostility and aggressiveness-related scales) and 20 items (socialisation scale). The majority of scales contain ten items. Each item is scored from 1 (“Does not apply at all”), through 2 (“Does not apply very well”) and 3 (“Applies pretty much”) to 4 (“Applies completely”), and the item scores are summed into a scale score. (Some items have a reversed scoring in which 1 corresponds to “Applies completely” and 4 corresponds to “Does not apply at all.”)

The KSP are not intended to cover “the whole personality” but rather to measure certain vulnerability factors that underlie aspects of psychopathology, especially psychopathy

(Schalling, 1978). The scales are divided into five groups covering aspects of extraversion (impulsiveness, monotony avoidance, and detachment), social conformity (socialisation, and social desirability), emotional instability (somatic anxiety, muscular tension, psychic anxiety, psychasthenia, and inhibition of aggression), aggressiveness (verbal aggression, indirect aggression, and irritability), and hostility (suspicion, and guilt).

Psychasthenia is based on validity (with reversed scoring), and detachment is based on concepts of stability derived from Sjöbring's personality dimensions. All aggressiveness and hostility scales are adapted from the Buss-Durkee Hostility Inventory (Buss, 1961), and it is assumed that they reflect diverse tendencies (strategies) for coping with aggressiveness-related situations: indirect aggression reflects a tendency to react with undirected anger; verbal aggression includes arguing, shouting, and being overly critical; irritability reflects a tendency to irritation; suspicion includes the projection of ill-will onto others; and guilt reflects aggressiveness with or without guilt feelings.

The socialisation scale is based on items from the Gough Delinquency scale (Gough, 1960), theoretically linked to psychopathy. The content analysis of the socialisation scale may indicate, however, that this scale reflects negative childhood experiences, poor school and family adjustment, social isolation, and current general dissatisfaction, rather than indicating psychopathy.

The construction of two different types of anxiety scales: somatic anxiety (a tendency to react with autonomic disturbances, distress, and panic) and psychic anxiety (a tendency to worry), was based on a two-factor theory of anxiety (Buss, 1962; Schalling et al., 1975).

Generally, the KSP scales show a good stability over time and between situations (for a review, see Gustavsson, 1997). Long-term (10 year) test-retest reliability in noncriminal adolescents showed good stability on all KSP scales, ranging from .53 to .73 (Kampe, Edman, & Hannerz, 1996). Stålenheim (1997), in a study on male offenders referred for an FPE, reassessed the subjects after about two years in order to study the change in their personality traits measured by the KSP. She also found good stability on all KSP scales with test-retest coefficients that ranged from .41 to .81, in spite of the fact that these offenders were assessed in two different situations, under an FPE in one case, and outside of the forensic psychiatric department (within a community or in prison) in the other case.

Gustavsson (1997) examined the validity and reliability of scales from the KSP and showed that the majority of the scales, with the exception of several aggressiveness-related scales, are reliable and valid (for a review, see also Dåderman, 2002b, Table 2, p. 22). (For a review discussing the predictive and discriminant validity of the KSP, focused on substance use disorders, see the *Introduction*.) Both hostility-related scales (guilt and suspicion) have consistently demonstrated poor reliability in terms of internal consistency, measured by Cronbach's alpha (e.g., Engström, 1997; Gustavsson, 1997; Malgir, 2004; Gustavsson, Weinryd, Göransson, Pedersen, & Åsberg, 1997; af Klinteberg, Schalling, & Magnusson, 1986; Persson, 2002).

In the present sample of juvenile delinquents (Studies I and IV), reliability was good for the majority of the KSP scales (Dåderman, 2002b). Cronbach's alpha was .75, .67, .84, .80, .81, .67, and .68 for the impulsiveness, monotony avoidance, socialisation, somatic anxiety, muscular tension, psychic anxiety, and verbal aggression scales. For the remaining scales, Cronbach's alpha showed poor reliability; it ranged from .26 (suspicion scale) to .59 (social desirability scale). In the present sample of offenders referred for an FPE, Cronbach's alpha was good for all KSP scales with a few exceptions. The exceptions were guilt, suspicion,

irritability, and indirect aggression scales; Cronbach’s alpha ranged from .32 to .57 for these scales. Cronbach’s alpha was .87, .79, .82, .61, .78, .82, .73, .62, .85, .78, and .74 for the somatic anxiety, psychic anxiety, muscular tension, social desirability, impulsiveness, monotony avoidance, detachment, psychasthenia, socialisation, verbal aggression, and inhibition of aggression scales, respectively.

*Psychopathy Checklist–Revised (PCL-R) (Study IV)*

Hare (1980) developed a method for screening criminals for psychopathy. This method uses an instrument known as the “Psychopathy Checklist”, which was later revised (PCL-R; Hare, 1991, 2003). It consists of 20 items, scored 0, 1, 2, or “omit”; 2 indicates that the item definitely applies, 1 indicates that it may or may not apply (it applies to a “certain extent, but not the degree required for a score of 2”), and 0 indicates that it does not apply. If there is insufficient information from an interview and from examination of the file to score an item, the item is omitted. Up to five items may be omitted without invalidating the total scores. Scoring of each item yields a score on one of the two factors described below. The scoring also yields scores on the four facets described below, and a total score. Extensive item descriptions are given in the manual and in the PCL-R rating booklet (Hare, 2003), to assist the clinician or researcher who assesses (scores) psychopathy.

Table 6 presents the items in the PCL-R, with the focus on the modified version (Forth et al., 1990), which was used to rate psychopathy in the juvenile delinquent sample described in this thesis.

Table 6

*Item descriptions of the Hare Psychopathy Checklist – Revised (PCL-R) (Hare, 2003), including information about the items that have been modified for rating psychopathy in the juvenile sample (Dåderman & Kristiansson, 2003, 2004, Study IV), according to Forth et al. (1990)*

Item <sup>1</sup>	
1. Glibness/Superficial charm (1)	11. Promiscuous sexual behaviour <sup>2</sup>
2. Grandiose sense of self worth (1)	12. Early behavioural problems (4)
3. Need for stimulation/Proneness to boredom (3)	13. Lack of realistic long-term goals (3)
4. Pathological lying (1)	14. Impulsivity (3)
5. Cunning/Manipulative (1)	15. Irresponsibility (3)
6. Lack of remorse or guilt (2)	16. Failure to accept responsibility (2)
7. Shallow affect (2)	17. Many short-term marital relationships <sup>2</sup>
8. Callous/Lack of empathy (2)	18. Juvenile delinquency (4) <sup>3</sup>
9. Parasitic lifestyle (3) <sup>2</sup>	19. Revocation of conditional release (4)
10. Poor behavioural controls (4)	20. Criminal versatility (4) <sup>4</sup>

*Notes.* <sup>1</sup>Figures within brackets refer to the four PCL-R facets; the items without figures do not load on any factor; 1 = “Interpersonal”; 2 = “Affective”; 3 = “Lifestyle”; 4 = “Antisocial”. <sup>2</sup>A modified item (omitted). <sup>3</sup>A modified item – all violent offences (including charges or convictions for murder, attempted murder, manslaughter, sexual assault, assault causing bodily harm, robbery, weapons offences, kidnapping, and arson) were scored as 2, and nonviolent offences as 1 (none of the participants received a rating of 0 on this item). <sup>4</sup>A modified item – four or more types of offence were scored as 2, three types of offence as 1, and one or two types as 0 (only crimes committed up to the date of the PCL-R interviews were included).

A score of 30 or above is considered to confirm a diagnosis of psychopathy, according to the manual (Hare, 2003). Some researchers (e.g., Cooke, 1998; Cooke & Michie, 1999; Grann, Långström, Tengström, Stålenheim, 1998; Haapasalo & Pulkkinen, 1992; Rasmussen & Levander 1996) have suggested, however, that lower PCL-R scores (cut-off points of 25-26) should be used to fulfil the criteria for psychopathy in samples from Europe, especially when psychopathy is rated on the basis of file data only. This view is also presented in the Second Edition of PCL-R, Swedish version (Hare, 2003). PCL-R has become the gold standard for screening for this syndrome in forensic and correctional settings (Fulero, 1995; Stone, 1995). The validity of the PCL-R is good and well-reviewed in the manual (Hare, 2003).

It has been claimed that the PCL-R measures interpersonal and affective personality traits and socially deviant behaviour. Items are scored on the basis of an extensive file-review and a semi-structured interview. The PCL-R ratings are intended to reflect a person's typical functioning throughout life.

Factor analyses performed on different samples have arrived at a 2-factor solution (e.g., Cooke, 1995; Harpur, Hakstian, & Hare, 1988; Harpur, Hare, & Hakstian, 1989; Hobson & Shine, 1998; Kosson, Smith, & Newman, 1990; Marshall & Cooke, 1999; Moltó, Poy, & Torrubia, 2000; Reiss, Leese, Meux, & Grubin, 2001). Thus, the original PCL-R comprises two factors (Hare, 1991). Factor 1 (Selfish, callous, and remorseless use of others) comprises eight items that reflect the more classic characteristics of psychopathy (e.g., lack of empathy and guilt, manipulativeness, superficial charm), whereas Factor 2 (Chronically unstable, antisocial, and socially deviant lifestyle) comprises nine items that contain the more behaviour-based features of poorly socialised conduct characteristics (e.g., early behavioural problems, impulsiveness, irresponsibility).

Cooke and Michie (2001) postulated that the PCL-R measures more than two factors. According to their 3-factor model of psychopathy, including only 13 out of 20 PCL-R items, the psychopathic personality domain comprises components that they named "Arrogant and deceitful interpersonal lifestyle" and "Deficient affective experiences". Both of these factors comprise four items each. The model eliminates several items that are more closely tied to criminal behaviour from the traditional Factor 2 in the 2-factor model, and proposes a new domain, named "Impulsive and irresponsible behavioural style", comprising five items. Thus, this model is more personality-oriented than the traditional 2-factor model. Recent studies (e.g., Kosson, Cyterski, Steuerwald, Neumann, & Walker-Matthews, 2002) of the factor structure of the PCL:YV support the 3-factor model. A Swedish study of almost 300 severe violent offenders sentenced to prison (Johansson, Andershed, Kerr, & Levander, 2002) has also confirmed the three-factor model.

The recently published Second Edition of Hare's PCL-R (2003) describes a modified factor structure. Factor 1 is still described as Interpersonal/Affective. It contains Facets 1 and 2, while the original Factor 2, now labelled Social deviance, comprises Facets 3 and 4. The four facets are labelled Interpersonal, Affective, Lifestyle, and Antisocial. It should be noted that Facets 1, 2, and 3 are identical to those of the 3-factor model of psychopathy proposed by Cooke and Michie (2001). Spain et al. (2004) stated that: "recently, a four-factor structure of the revised PCL-YV (Forth et al. 2003), which loads only 18 of the original 20 items, has been endorsed by the authors of the PCL:YV" (p. 89). The first three factors are identical to the 3-factor structure found by Cooke and Michie.

Reliability data presented in the PCL-R manual show that the reliability of the PCL-R is adequate (Hare, 1991, 2003). Results from studies on psychopathy in different samples and in different countries have confirmed that the inter-rater reliability and internal consistency coefficients of the PCL-R are high (as indicated by a Cronbach's alpha or intraclass correlation coefficients (ICC)<sup>11</sup> above .80, Cohen's kappa<sup>12</sup> or a weighted kappa for concordance between raters ranging from .50 to 1.00, and 70-100% agreement on diagnoses of psychopathy between raters). Similar values have been obtained in different countries (e.g., Brandt et al., 1997; Grann et al., 1998; Hobson & Shine, 1998; Hume, 1997; Molto et al., 2000; Reiss et al., 2001; Ridenour, Marchant, & Dea, 2001; Strachan, 1995). Because of the good psychometric properties of the instrument and its high predictive validity, the PCL-R has been used, together with other instruments, as a measure of risk assessment.

In the present samples of participants, both the ICC and Cohen's kappa (cut-off 30) indicated that the PCL-R ratings in both groups were highly reliable. The ICCs for the total scale score were .89, .90, and Cohen's kappa was .69, .64, in the forensic psychiatric (Dåderman, 2005), and in juvenile delinquent samples (Dåderman & Kristiansson, 2003), respectively.

## Procedure

### *Design and qualitative interviews*

The studies described in this thesis were of mixed design, having both a *prospective* (longitudinal) nature and a *retrospective* nature. The decision to pool the data from two samples into one was a conscious decision. The interviews assessed, among other things, personality traits and psychopathy, and substance use disorders, with a focus on FZ abuse. I have been carried out the qualitative interviews for all FZ abusers from both samples. These interviews lasted from approximately half an hour to two hours, depending on how articulate the participant was, his age, and the duration and intensity of the abuse of FZ. Generally speaking, the in-depth interview for each participant commenced in a topic-relevant, but essentially non-directive, open-ended, and broadly structured manner. As the interview progressed, depending on the richness or the paucity of information being obtained, the style became more specific, closed, and narrowly structured. Information that emerged from the interviews was transcribed and labelled systematically in the form of quotations. The main findings were typically comments relating to FZ abuse and to intoxication with FZ (see also the subsection *Qualitative analysis*).

The procedures used for the two samples are described in more detail below.

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<sup>11</sup> The ICCs (see Shrout & Fleiss, 1979) assess rating reliability by comparing the variability of different ratings of the same subject to the total variation across all ratings and all subjects. They are commonly used when the data are continuous. The ICCs range from 0 to 1, and there is no consensus in the literature concerning ranges for rating reliability as "acceptable" and "unacceptable". There are different classes of ICC for reliability.

<sup>12</sup> Cohen's kappa is a measure of rater agreement, often used when data are dichotomized (yes, no). It ranges from -1 (perfect disagreement) to 1 (perfect agreement). It is generally accepted that kappa values greater than .75 indicate good reliability, those between .50 and .75 indicate fair reliability, and those below .50 indicate poor reliability (Spitzer, Fleiss, & Endicott, 1978).

### *The forensic psychiatric sample*

Participants were studied during one year (November 1997 - November 1998). An in-depth interview regarding FZ abuse was carried out with each participant. All participants were interviewed by me in a room at the Department of Forensic Psychiatry in Stockholm. Reading achievement and writing skills, neuropsychological functions and cognitive functions, self-confidence, and psychopathy were all also assessed individually. The period of time spent with each participant ranged from eight to 16 hours.

Blood samples for the determination of platelet MAO activity were obtained at the department and sent for analysis to Lars Oreland at the Department of Neuroscience, Division of Pharmacology at Uppsala University in Sweden (data not yet reported).

Most participants also completed a number of self-reported inventories (see above). The participants filled in the inventories while in their own rooms, located in the closed assessment and observation section of the department. Items were read aloud to those five participants who showed severe difficulties in completing the inventories. Some participants did not complete the inventories. Two of these participants could not read Swedish sufficiently well, one had a major depressive episode, and three others became psychotic. Other participants refused to fill in the inventories. A few single missing values were replaced by the mean of the valid responses to the other items in the pertinent scale. One participant had more than 5% of the responses in the KSP missing, and therefore his responses concerning this particular inventory (KSP), have been excluded. This left 47 (the KSP), 48 (the MNT), and 49 (the EPQ-I and SSS-V) cases for analyses.

The official files were also examined (see above).

The ratings procedure of the PCL-R scores has been described elsewhere (Study IV; Dåderman, 2005). In brief, clinicians from the Department of Forensic Psychiatry and I diagnosed whether 43 of the 60 offenders undergoing an FPE were psychopathic (both interviews and file data were used by all raters), while my research assistant (Jenny Laurell, JL)<sup>13</sup>, and I diagnosed the remaining 17 participants (JL used only file data, while I used both interviews and file data). A research assistant rated the remaining participants, rather than clinicians from the Department of Forensic Psychiatry, since not all clinicians were educated in the rating of psychopathy, and those who were educated refused to rate the remaining sample of 17 participants.

Before collecting the data for the project on the forensic psychiatric participants described above, we asked the clinicians if they were interested in carrying out case studies regarding intoxication with FZ in cases of severe violent crimes, with the intention of including these case-studies in the project (Study III; Dåderman et al., 2003).

### *The juvenile delinquent sample*

The personalities and mental health of the participants were studied over a 6-week period (January 1996 - March 1996) at the institutions in which the juvenile was being held, and an in-depth interview regarding FZ abuse was carried out with each participant. All juvenile delinquents confined in these institutions during this period were invited to participate, even if they were on medication or were likely to have difficulty in reading the questionnaires.

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<sup>13</sup> JL is a doctoral student trained in the use of the PCL-R by me as part of a postgraduate course, "Retrospective rating of psychopathy (PCL-R), using file data only", held at the Department of Psychology, Stockholm University.

Juveniles confined only on a short-term basis were also invited to take part. It was strongly emphasised that participation was voluntary and could be interrupted at any time. Two juveniles declined to participate after hearing a description of the research project.

All the interviews and assessments were carried out in the participants' own rooms, or in a special visiting room. Each participant was asked if he had previously been diagnosed as dyslexic (or if he had difficulty in reading the questionnaires). All participants completed a number of self-reported inventories (see above). Items were read aloud to ten participants who showed difficulty in completing the inventories. Almost 10% of the remaining participants displayed obvious symptoms of severe dyslexia, reading the questionnaires very slowly. Whenever a participant reported that an item was difficult to understand, the item was explained using other words. I prepared a special "dictionary", which consisted of a list of words "translated" into the colloquial language often used by criminals and abusers. Some difficult words from the personality inventories were explained in the dictionary. The dictionary was compiled before the study, in collaboration with a small sample of young men from a juvenile group (for details see Dåderman, 1996, Appendix).

Each participant was given an identification number, and responses from all participants were noted in writing. There were many breaks in the interview sessions, as a result of boredom, hunger, and a recurrent craving for smoking (all subjects except two smoked cigarettes). The period of time spent with a participant ranged from two to seven hours.

The rating procedure for the PCL-R scores has been described elsewhere (Dåderman, 2002b; Dåderman & Kristiansson, 2003). Each participant received PCL-R assessments from one rater (me). The assessments were based on the file information, together with an extensive interview. The interview regarding psychopathy ratings in the group of 47 juvenile participants was carried out during the same session as a great deal of demographic information was collected (Dåderman, 1996), combined with an interview (structured and in-depth) regarding substance use disorders, with a focus on FZ abuse. The interviews for the additional group of nine juvenile participants were designed separately and carried out between November 1997 and November 1998. The PCL-R interview took from 90 to 120 minutes, and the collateral review from 60 to 120 minutes. After this was completed, each of the 20 PCL-R items was rated using the above-described modified version of the PCL-R (Forth et al., 1990). The Hare Psychopathy Checklist: Youth Version (Forth et al., 2003) was not used, because this instrument was not available in Sweden at the time of the assessments. The modifications were necessary because the delinquent participants were, naturally, young, and many had been within correctional institutions for many years. This meant that many had restricted experience, and so we omitted Item 11 (promiscuous sexual behaviour). Two types of potentially deviant behaviour important for Item 19 (revocation of conditional release) were defined. An escape from a correctional institution aggravated by drug or alcohol misuse or by reoffending (or by both) while escaped scored as 2, while a "simple" escape scored only as 1 (see Table 6 for a detailed presentation of the 20 PCL-R items).

Omitted items were replaced by mean values based on the expected total score given by tables in the PCL-R manual, a procedure known as "prorating" (Hare, 1991).

A second rater (M. Kristiansson, my present main supervisor in forensic psychiatry), who was blind to the scores given by me, rated twenty-eight participants (50% of the total sample). Both raters received training in the use of the PCL-R from David Cooke, who is an internationally recognised expert in its use, and both attended a conference on psychopathy arranged by Robert D. Hare. In addition, M. Kristiansson received training in PCL-R rating

from Steve Hart, and I attended a workshop on psychopathy arranged by Jennifer Skeem. Both Steve Hart and Jennifer Skeem are internationally recognised experts on the use of the PCL-R. Both raters have worked with both juvenile and adult offenders. Inter-rater reliability coefficients for the PCL-R were assessed using a subset of the 28 cases. The final PCL-R scores for the 28 participants in the subset were obtained by averaging the scores of the two independent raters.

## **Treatment of data and statistical analyses**

### *Qualitative analysis*

The data from the in-depth interviews consisted of direct quotations from the 19 juvenile delinquent FZ abusers and the 18 forensic psychiatric FZ abusers regarding their experiences, opinions, feelings, and knowledge of being frequently intoxicated with FZ. Glaser and Strauss (1967) describe the purest form of the grounded theory approach to data analysis, and they explain that this approach assumes that all explanations (or theories) are derived from the sampled qualitative data *itself*, rather than from other sources (i.e., without reviewing the literature on a research question) or the researcher's prior theoretical viewpoint. Study I describes the use of the grounded theory in its almost pure form, because the attempted review gave no relevant references about the issue studied. Thus, no ideas concerning the content of the data were formulated before collecting the data.

The first step in achieving theoretical sensitivity (Study I) was to analyse the interview notes with as few predetermined ideas as possible. Three main steps in coding were used, as recommended by Glaser (1978): a preliminary data categorization by general topic of interview content ("open coding"), followed by "substantive (selective) coding" and, finally, "theoretical coding" (basic social-psychological process). Open coding is a process involving simultaneously generating of research codes for pre-defined and emergent categories to sort segments of the text that concerning specific themes. For example, open codes identifying parts of the text in which the FZ abusers discussed how their personality become changed, were coded into a substantive code, labelled "Change of personality". Substantive coding involved three stages: the text was re-examined, concepts (core categories) reflecting the social-psychological process of FZ abuse were identified, and their nature and relationships were explored in detail using Strauss and Corbin's (1990) question, "What is this an example of?" (p.63). Categories, their relationships, and exemplifying quotations were recorded in detailed memos. As interviewing continued, new attempts to discover information ("probes") were made to test theoretical relationships. The "final" major categories with exemplifying quotations are illustrated in Figure 5. The figure is an attempt to visualise the steps used, the first of which was open coding (data were compared and contrasted), following which all similar phenomena were grouped into four broader categories (substantive coding), which were labelled. Selective coding and theoretical coding followed (Strauss & Corbin, 1990), during which core categories (central phenomenon) and the basic social-psychological process emerged. (It should be noted that my co-author and I have not submitted this figure for publication, because we plan to include the one new category that emerged from qualitative interviews carried out with the forensic psychiatric FZ abusers (data not reported). This manuscript is still in preparation).

Multiple coding concerns the same issue as quantitative equivalence in inter-rater reliability, and it involves the cross-checking of coding strategies and the interpretation of data by independent researchers. I discussed the emergent coding segment with other doctoral students and with the leader of a course in grounded theory during Study I<sup>14</sup>. Triangulation addresses the issue of internal validity by using more than one method of data collection to answer a research question. I considered this validity criterion to be difficult to fulfil, but observations of behaviour in another reference group of FZ abusers may have compensated for it. Quantitative comparisons were also carried out (see below). The last technical procedure that can be used to evaluate qualitative methods is respondent validation. This technique involves cross-checking interim research findings with the respondents. Barbour (2001) describes the ready appeal of this technique, while Mays and Pope (2000) have pointed out that researchers seek to provide a more general theory, while the responders may have personal and individual concerns. It is difficult to avoid or correct any “romanticising” of the responders’ accounts. Further, it was impossible to plan this form of validation in the design of the studies described here.

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<sup>14</sup> Directly after the data sampling (1996), I attended a qualitative course that focussed on grounded theory: “Qualitative research methods: Analysis and design”, held at the Department of Psychology, Stockholm University. The course leader was Svante Hovmark.

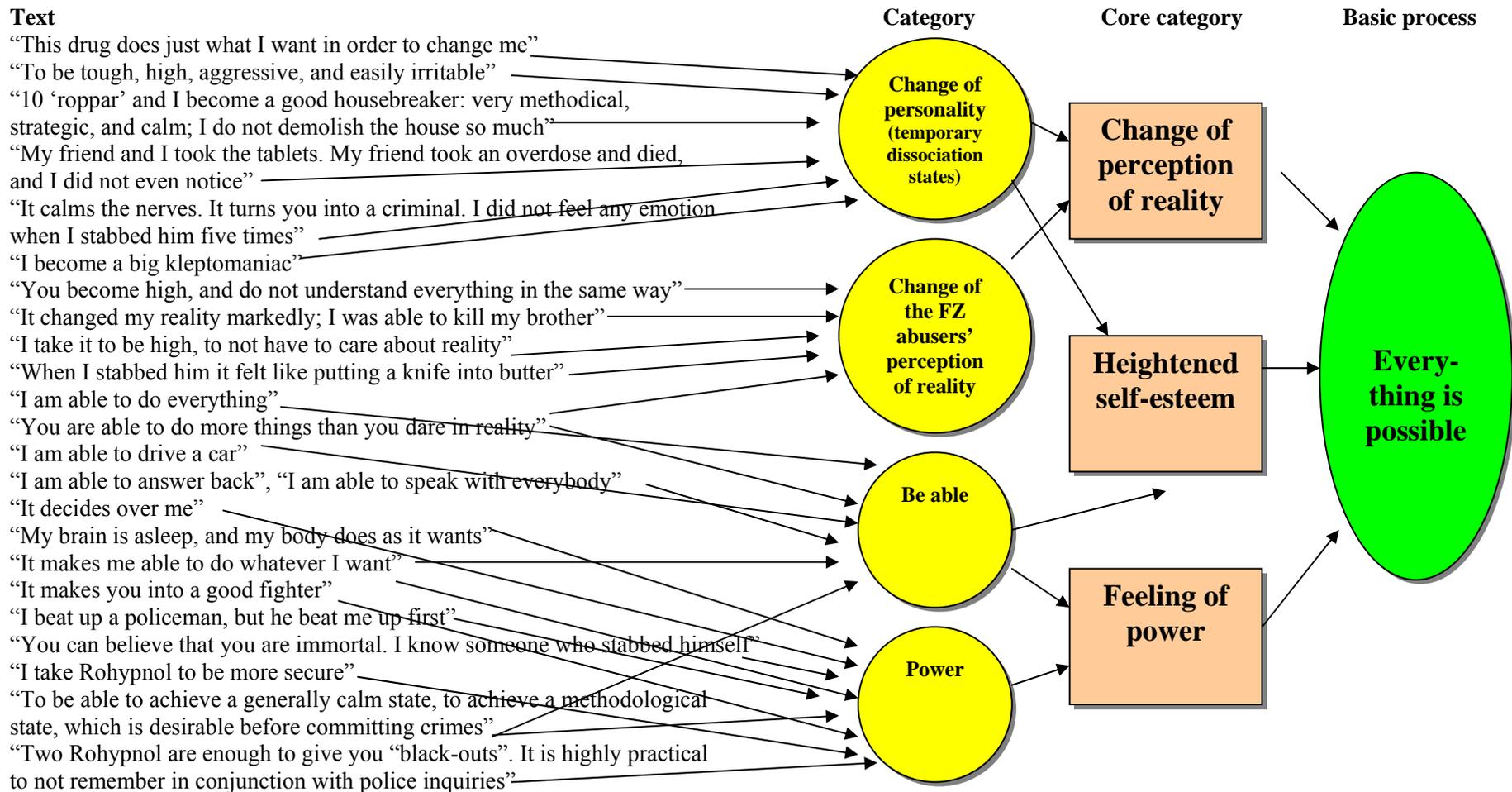


Figure 5. Relationships between text and categories, and the process, using a “grounded theory” analysis (Glaser & Strauss, 1967), of finding the appropriate answer to the question: “Why do FZ abusers abuse just FZ (and not another substance)?”. The figure illustrates the steps used, the first of which was open coding (data were compared and contrasted), after which all similar phenomena were grouped into four broader categories, which were labelled (substantive coding). Selective and theoretical coding followed (Strauss & Corbin, 1990), during which core categories (central phenomenon) and the basic social psychological process emerged. The idea of presenting the coding process and the analysis in this way has been adapted from Beck (1993) and from Kearney, Murphy, Irwin, and Rosenbaum (1995).

## *Statistical analyses*

The mean and standard deviation were calculated for all data. Kurtosis and skewness were calculated to examine the distributions of the PCL-R scales. The Levene's test, which is the most commonly used test, was used to test whether the variances of the two populations were equal. A two-tailed *t*-test for independent samples (Study II) or a one-way analysis of variance (ANOVA) (Study I) was subsequently used to test whether the means of parametric data were equal. These two statistical values are strictly univariate in nature and are often used in psychology to determine whether two means (Student's *t*-test or ANOVA) or two or more means (ANOVA) are significantly different. The mean score items for the 20 individual items of the PCL-R were initially entered independently, and Student's *t* was calculated for these items (Study V). They were then subjected to a discriminant analysis (Tabachnick & Fidell, 1996). These calculations enabled us to discover differences between FZ abusers and non-FZ abusers in the mean scores of the 20 individual PCL-R items.

Bonferroni's correction (Howell, 1997) was not routinely used in the work described in this thesis. A note is, however, presented when appropriate (see Study II), about the alternative interpretation of a significant result *if* this correction was used. Howell proposes that: "when we have completed running a set of comparisons among our group means, we will arrive at a set (often called a *family*) of conclusions" (p. 349). Bonferroni's correction can be used for adjusting the selected alpha level to adjust for the overall type I error<sup>15</sup> rate. The procedure involves computing the adjusted rate  $A = 0.05/b$ , where *A* is adjusted rate that uses as the critical value in each separate test, and *b* is the number of statistical tests to be performed.

This thesis used the T-scores of normative personality values (from a "normal" population) in order to compare the mean personality scale scores of the groups of participants with the normal distribution of means (Studies I, II and IV). The parameters compared in this way were T-scores for the KSP, EPQ-I, SSS-V, and PCL-R; and Standard scores for the MNT. (T-scores for the KSP and EPQ-I are derived from the raw data following adjustment for age and sex.) All raw values on each scale of each participant were transformed into T-scores. These calculations were based on the means and standard deviations of a group of 200 randomly selected subjects from the greater Stockholm area (Bergman et al., 1988). Similar transformations were carried out for the MNT and SSS-V scales, using male groups as references (Nyman & Marke, 1962; Zuckerman, 1994). T-scores for the PCL-R T-scores measured in Study V have been derived from the raw scores on the normative ("normal") population of North American male offenders ( $N = 5408$ ) (see T-score tables and a discussion regarding T-scores, Hare, 2003, Chapter 9). All raw values on each facet of each participant were transformed into T-scores.

Kendall's coefficient of concordance, also known as "Kendall's *W*" (Howell, 1997), was used to test the association between nonparametric variables when testing for differences between groups (FZ abusers vs. non-FZ abusers) with different

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<sup>15</sup> According to Howell (1997) a Type I error (rejecting the null hypothesis when in fact it is true) is called a Type I error, and "its conditional probability (the probability of rejection the null hypothesis given it is true) is designed as  $\alpha$  (alpha), the size of rejection region" (p. 99). Another definition of Type I error is given by Brace, Kemp, & Snegler (2003); "Type I error involves incorrectly rejecting a null hypothesis, thus concluding that there is a significant effect when in fact the means differ due to chance (p. 195).

background characteristics (Study I). Kendall's *W* ranges between 0 (no association or agreement) and 1 (complete association or agreement).

Pearson's Chi-squared method was used to test the significance of non-parametric variables when testing for differences in frequencies in properties between the groups (juvenile delinquents vs. forensic offenders) (Studies II and IV, and Comments to Study I).

The main five substance use types in the samples studied were alcohol, cannabis or marijuana, FZ, amphetamines and/or cocaine, and opiates (Studies I and II; Dåderman, 2002b; Trygg, 2000). A correlation matrix using Kendall's tau correlation coefficients was developed in order to describe possible associations between the scores on the four facets of the PCL-R and these main five substance use disorder types.

The internal consistency of the PCL-R was evaluated by means of Cronbach's alpha, and the homogeneity was evaluated by mean interitem correlation coefficients.

In order to examine relationships between the four facets of psychopathy, group membership and FZ abuse, a stepwise logistic regression analysis (forward) was performed with FZ abuse as the dependent variable, and the four facets of the PCL-R and group membership (the juvenile delinquent group or forensic psychiatric group) as independent variables, with an inclusion level of 5% (Study IV). Each facet of the PCL-R was dichotomised using a cut-off T-score of 61. A value of T-score of 61 was used as the cut-off because it is commonly accepted in clinical practice that psychological scale scores between T-scores of 40 and 60 are within a "normal range", while T-scores above 60 reflect deviance.

A forward stepwise logistic regression analysis was also carried out using the 20 items of the PCL-R as independent variables and FZ abuse as the dependent variable.

All statistical analyses were carried out using the Statistical Package for the Social Sciences (SPSS), different versions (e.g., Version 11.5 in Study IV) for Windows.

## **Ethics**

All participants received verbal and written information about the purpose and design of the projects. All relevant authorities (including the staff at the institutions, the staff at the Department of Forensic Psychiatry in Stockholm, the Swedish National Board of Forensic Medicine, and the Swedish National Police Board) were approached and permission to carry out the investigations was obtained. The projects received approval by the Research Ethical Committees at the Karolinska University Hospital, Huddinge, and at Uppsala University.

## **MAIN FINDINGS AND COMMENTS**

### **Study I**

*Prevalence of FZ abuse, combination of FZ with other substances, and possible group differences in the type of substance abuse*

Nineteen out of 47 (40.4%) of the juvenile delinquent participants abused FZ. FZ was taken, with one exception, in the absence of medical supervision, in amounts ranging

from two to six milligrams on any one occasion, which was reported to be a “desirable” dose. FZ was used solely or in combination with alcohol, and/or in combination with other legal or illegal substances, such as other benzodiazepines (e.g., diazepam, oxazepam, or nitrazepam), cannabis, amphetamines, opiates, anabolic steroids, LSD, or ecstasy (see Study I, Table 3, p. 94). Rohypnol was one of the most commonly abused compounds that include FZ: 30% of the FZ abusers (6 out of the 19 FZ abusers) used only Rohypnol, while the remaining 13 FZ abusers used Fluscand, Flunitrazepam, and Flupam in addition to Rohypnol.

Study I describes the use of Kendall’s coefficient of concordance,  $W$ , in order to test the association between different variables and FZ abuse (here: type and extent of substance abuse for specific drugs, see Study I, Table 3, p. 94). The results show that FZ abuse was not significantly associated with any type of substance abuse (see the *Comment* below).

#### *Comment*

The results obtained in Study IV and subsequent reflections derived from clinical reality have stimulated a deeper re-examination of the data from Study I (see Table 1), using the Chi-squared test instead of Kendall’s  $W$ . This re-examination has shown that FZ has a significant association with several variables (see also the *Comment* in the *Crime differences* subsection), and several alternative conclusions can be drawn (see below).

There were significant associations between FZ abuse and the abuse of amphetamines and/or cocaine, cannabis, and opiates, Chi-squared = 4.91, 18.83, and 12.32;  $df = 1$ ,  $p = .03$ ,  $< .00045$ , and  $< .00045$ , respectively (the sum of data for the frequency of abuse “often” and “every day”, suggesting substance abuse according to DSM-IV, presented in Study I, Table 3, respectively, were used for this analysis).

FZ abuse does not have a significant relationship with alcohol abuse or dependence, Chi-squared = 1.34,  $p = .25$  (the data presented in Study I, Table 3, row 1, were used for this analysis). Other specific substances (anabolic steroids, LSD and ecstasy) were abused at low frequencies, and improved analyses were not carried out to examine possible associations between FZ abuse and the abuse of these substances.

#### *Alternative conclusion*

FZ abuse has a significant association with amphetamine and/or cocaine abuse, cannabis abuse, and the abuse of opiates.

#### *Why do juvenile delinquents abuse just FZ (and not another substance)?*

Grounded theory analysis was used to find the answer to the question above (see *Methods*, Figure 5). The main three core categories (central phenomena), which have been labelled: “change of reality”, “heightened self-esteem”, and “feeling of power”; and the basic social psychological process, which has been labelled “everything is possible”, emerged from the data (i.e., from the qualitative interviews). The main reason for abusing FZ, thus, was to obtain an increased feeling of power and self-esteem, a feeling that everything is possible (typified by the comments: “This drug does just what I want in order to change me. It is so much stronger, I am able to do

everything”, “My brain is asleep, and my body does as it wants”). In summary, FZ abusers have the experience that reality changes. The majority of abusers also reported that FZ reduced their level of anxiety. The feeling that everything was possible was considered as an overarching basic social psychological process. FZ abusers said that they preferred FZ over other substances, including other benzodiazepines such as diazepam, oxazepam, or nitrazepam, and thus, this feeling (that everything is possible) was specifically ascribed just for FZ.

*Do their traits, behaviour or other psychiatric/psychological characteristics change while intoxicated with FZ?*

In order to study possible psychiatric adverse effects of FZ, with a focus on violent behaviour during intoxication with FZ, the juvenile delinquent FZ abusers were used as “experts”. They were polysubstance abusers and could describe precisely the effects that different substances had on their behaviour and psychiatric state.

All of the FZ abusers experienced changes in reality and/or i personality (temporary dissociation states) while intoxicated with FZ. This experience varied from person to person and from occasion to occasion. For example, the FZ abusers reported that FZ seems to reinforce a state that was experienced prior to the intoxication. The abusers displayed hostile and frightening behaviour while intoxicated with FZ, often resulting in brutality: they became cold-blooded, experienced feelings of enormous strength, and were able to achieve a generally calm, non-anxious, and methodical state of mind. They described how FZ reduces fear and insecurity, and stimulates the belief that nothing is impossible. According to their statements, this was related to unprovoked, violent crimes. Moreover, FZ abusers showed no guilt about their violent offences (“When I stabbed him it felt like putting a knife into butter”) (see Figure 5 for more quotations). In conclusion, it can be stated that all FZ abusers, while intoxicated, considered the dysfunction of fundamental innate emotional reactions, such as anger, fear, disgust and sadness, as a desirable effect. The following quotations exemplify this: “I didn’t feel any emotion when I stabbed him five times”, “My friend had taken an overdose and died, and I didn’t even notice”. Such dysfunction was experienced by all FZ abusers and was described both as frightening and as highly exciting, accompanied as it was by a heightened sense of power and self-esteem.

The most common adverse effect of FZ was complete or partial amnesia, particularly if the FZ was taken in combination with alcohol. This caused a severe disturbance in perceptual and cognitive processes (“black-out”), sometimes lasting for two weeks. The majority of the juvenile delinquent FZ abusers considered this to be highly practical in connection with police inquiries.

*Subjective differences between the experience of intoxication with FZ and with other benzodiazepines*

All FZ abusers sometimes abused other benzodiazepines and many of them abused other substances than FZ and they could therefore describe several differences between benzodiazepines from their own perspective. One difference was the positive (i.e., physically nondangerous) combination of FZ with alcohol. According to FZ

abusers, other benzodiazepines combined with alcohol could be physically “dangerous,” because the abusers could experience breathing difficulties and palpitations. It is possible to take five to six milligrams of FZ, and still be capable of driving. In addition, FZ was more effective in reducing anxiety than other benzodiazepines.

#### *How do FZ abusers get access to the drug?*

Juvenile delinquent FZ abusers obtained FZ on an illegal drug market, by stealing from a pharmacy, from retired men and women (often the abusers’ relatives) who were known to have FZ in their apartments, by stealing from other drug addicts (often elderly homeless men who sleep on night buses, having FZ tablets visible in their pockets), or from a supplier at parties (frequently available). The abusers reported that it was very easy to get this drug. Primary care physicians prescribed FZ only to two participants.

#### *Background demographic characteristics*

Kendall’s *W* was used in Study I to determine the association between FZ abuse and different variables. FZ abuse was not significantly associated with any demographic background factor (see the comment below, which includes results from subsequent improved analyses, and an alternative conclusion).

#### *Comment*

Subsequent re-examination of the data presented in Study I (see Table 1, p. 92,) using Chi-squared statistics indicates that FZ has a significant association with several variables (see also the *Comments* in some subsections below: *Crime differences*, and *Prevalence of FZ abuse, combination of FZ with other substances, and possible group differences in the type of substance abuse*).

There was a significant association between FZ abuse and immigrant background, Chi-squared = 6.85, *df* = 2, *p* = .03; seven out of the nine participants who had one parent with immigrant background were FZ abusers, while 16 out of the 22 participants who had both parents born in Sweden were non-FZ abusers. The data regarding any type of immigrant background have been subsequently collapsed, and 13 out of the 25 participants having some type of immigrant background were FZ abusers. This analysis shows that there was no significant association, Chi-squared = 2.97, *df* = 1, *p* = .09, between FZ abuse and having at least one parent with immigrant background.

There was a significant association between being an FZ abuser and the frequency of previous treatment occasions in a juvenile correctional institution, Chi-squared = 13.90, *df* = 2, *p* = .001; 13 out of 18 participants who had been resident at least three times in such an institution were FZ abusers, 11 out of the 16 participants who had received care one or two times were non-FZ abusers, while 12 out of these 13 participants who had never received care were non-FZ abusers. The association between FZ and recidivism into serious crime (see Appendix 1 for an explanation of Swedish legislation regarding juvenile delinquents during the period of this study) that

led to a new treatment period remained significant when all participants who had ever received care in such an institution were collapsed into one group, Chi-squared = 8.00,  $df = 1$ ,  $p = .005$ ; 18 out of the 19 FZ abusers had previously been sentenced to care in a correctional institution; 12 of these 13 participants who had never before received care, were non-FZ abusers.

There was a significant association between being an FZ abuser and having had contact with the psychological or psychiatric services during childhood, Chi-squared = 10.86,  $df = 1$ ,  $p = .001$ ; eight out of nine participants with such childhood contact were FZ abusers.

Data concerning abusers who had been “sentenced for violent crimes two or more times” (see Study I, Table 1, row 1) are based on self-reported information (the improved re-examination using Chi-squared statistics indicates a significant association between FZ abuse and this variable), but this data is misleading and should be removed from the table. These data were later compared with information in official files, and these files show that 13 out the 19 FZ abusers and 14 out of the 28 non-FZ abusers were sentenced to violent crimes two or more times, indicating no significant association between these two variables, Chi-squared = 1.57,  $df = 1$ ,  $p = .21$ .

Data regarding “metropolitan housing area” were also re-examined. There is a significant relationship between FZ abuse and this variable, Chi-squared = 4.9,  $df = 1$ ,  $p = .03$ .

There were too few participants in the groups to allow analysis of association between FZ abuse and other background demographic characteristics presented in Study I, Table 1.

#### *Alternative conclusion*

We conclude that FZ abuse has a significant association with childhood psychological/psychiatric contact, with having one parent with immigrant background, with living in a metropolitan housing area (Stockholm, Göteborg, or Malmö and the surrounding counties), and with recidivism into crimes leading to care in a juvenile correctional institution for serious offenders.

#### *Crime differences*

Juvenile delinquent FZ abusers did not significantly differ from juvenile delinquent non-FZ abusers (as determined by Kendall's  $W$ ) with respect to the number of different crimes committed. Some interesting figures did emerge, however. (See the comment below for a statistical re-examination of these data).

#### *Comment*

Subsequent re-examination of the data presented in Study I using Chi-squared statistics indicated, however, that FZ has a significant association with several variables (see Study I, Table 2, p. 93, and the *Comment* in the subsections: *Prevalence of FZ abuse, combination of FZ with other substances, and possible group differences in the type of substance abuse, and Background demographic characteristics*).

There was a significant relationship between FZ abuse and being sentenced with weapons offences, Chi-squared = 6.19,  $p = .01$ ; nine out of 13 participants with such sentences were FZ abusers. In addition, there was a significant relationship between FZ abuse and being sentenced with narcotics offences, Chi-squared = 14.57,  $p < .00045$ ; 11 out of 13 participants with such sentences were FZ abusers.

There was no significant relationship between FZ abuse and being sentenced for violent offences, theft offences, inflicting damage and arson, traffic offences, and other crimes; Chi-squared = 2.95, 0.001, 1.73, 0.76, and 1.87;  $p = .094, .98, .19, .38, \text{ and } .17$ , respectively. Seven out of 11 participants who were sentenced for robbery were FZ abusers. There was no significant relationship, Chi-squared = 3.21,  $p = .07$ , between FZ abuse and being sentenced with robbery, but the result was in the expected direction (see also Studies II and V).

#### *Alternative conclusion*

We conclude that FZ abuse has a significant association with weapons offences and narcotics offences.

#### *Personality traits in juvenile delinquent FZ abusers compared with juvenile delinquent non-FZ abusers*

The FZ abusers obtained mean raw scores on the KSP VA scale and on the SSS-V BS scale that were significantly higher than those of the non-FZ abusers ( $p < .01$  and  $p < .05$  respectively). The results are illustrated in Study I, Figures 1 and 2, p. 93.

## **Study II**

#### *Prevalence of FZ abuse and combination of the abuse of FZ with other substance abuse*

Eighteen out of 60 (30%) forensic participants were FZ abusers. FZ was often taken in combination with alcohol and amphetamines, cannabis, and other benzodiazepines, in the absence of *real* medical supervision. However, most of the forensic psychiatric FZ abusers had been prescribed FZ by their doctor.

#### *Why do the abusers abuse just FZ (and not another substance)?*

Forensic psychiatric FZ abusers gave several *different* reasons for being often intoxicated with FZ. The FZ abusers were therefore classified into three sub-groups, two of them based on the stated reason for the abuse, and one containing abusers who had suddenly decided to stop the abuse. The largest group ( $n = 8$ ) had a mean age of 28.8 years ( $SD = 4.6$  years) and consisted of participants who abused FZ to obtain an increased feeling of power and self-esteem (“to be able to do everything”). The second group ( $n = 7$ ) had a mean age of 26.0 years ( $SD = 6.5$  years) and consisted of participants who abused FZ to reduce their level of anxiety. The third group consisted of three participants who had become frightened by the unexpected properties of the FZ and decided to stop the abuse. Their decision to stop the abuse was based on the

brutality and the accompanying violent nature of crimes they committed under the influence of FZ, and on the fact that they had no memory of their crimes (anterograde amnesia).

*Do their traits, behaviour or other psychiatric or psychological characteristics change while intoxicated with FZ?*

Forensic psychiatric offenders who abused FZ, irrespective of their stated reason for the abuse, displayed hostile behaviour while intoxicated, they experienced the feeling of possessing enormous strength and became cold-blooded, which was reflected in unusual brutality of their violent crimes. It is interesting that some of the participants who used FZ in order to reduce anxiety reported an increase in anxiety, insomnia, excitation, nightmares, and in suspicion and irritability.

All FZ abusers reported the occurrence of anterograde amnesia after the consumption of FZ. In contrast to juvenile delinquent FZ abusers, forensic psychiatric FZ abusers experienced the loss of memory caused by FZ as very impractical and awkward in many situations.

*How do the FZ abusers obtain FZ?*

Forensic psychiatric FZ abusers obtained FZ from primary care physicians, who prescribed the drug without asking questions to determine whether the patient was psychologically or psychiatrically impaired. They often received the drug for other indications than insomnia, such as pain. (It should be noted that no participant has ever been diagnosed as having a sleep disorder, which is the only indication for FZ prescription. See Study II, Table 2, p. 35.) One participant reported that he could usually buy some empty prescription forms from his doctor at a price of 300 SEK (corresponding to approximately \$35 U.S.) for one form. (There are currently special prescription forms in Sweden for the prescription of FZ, with a watermark and a serial number.) He could therefore make up his own prescription for the desired quantity of FZ tablets. The subjects also satisfied their needs on the illegal market. Abusers often had an empty bottle that had previously held FZ tablets, with their doctor's name on the label. This bottle was then filled with tablets from the illegal market. This was practical if the abusers were arrested.

*Is FZ abuse reflected in psychiatric diagnoses?*

Only 4 out of 18 FZ abusers received a diagnosis of FZ abuse during an FPE.

*Background characteristics and possible associations between FZ abuse and any specific kind of crime*

Forensic psychiatric FZ abusers did not differ significantly from non-FZ abusers in the amount of actual convictions for violent offences (index crime FPE). The in-depth interviews revealed that most violent behaviour of FZ abusers did not result in criminal sentences. However, 13 out of 18 FZ abusers (72%) had been convicted of

violent offences in connection with the actual FPE (index crime), compared to 27 out of 42 non-FZ abusers (64%).

A number of variables did, however, differ significantly between forensic psychiatric FZ abusers and non-FZ abusers. These variables included the frequency of previous admission to an FPE; and convictions for robbery, weapons offences (usually involving a knife), narcotics-related offences and other crimes (such as theft). Five out of 18 FZ abusers (28%), compared to 2 out of 42 non-FZ abusers (5%), had been convicted of robbery in connection with the actual FPE. This is interesting as robbery and narcotics-related offences are crimes that are increasing in Sweden.

There were no differences between the FZ abusers and non-FZ abusers in the mean overall functioning on Axis V, using the GAF scale (see *Methods*).

### *Personality traits*

Many personality traits of forensic psychiatric participants differed from those of people in a normal population, suggesting psychiatric or psychological vulnerability. The participants' scores were very much lower than those of normative males on the solidity and validity scales of MNT and on the socialisation scale of KSP, while they were very much higher than those of normative males on the neuroticism and impulsiveness scales of EPQ-I, and on the experience-seeking scales of SSS-V. As expected, the participants obtained high scores on all anxiety-related scales, with one exception: the inhibition of aggression scale.

### *Personality traits in FZ abusers and in non-FZ abusers*

The mean T-scores on the anxiety-related scales for FZ abusers were not higher than those of non-FZ abusers (Study II), which may indicate that FZ was not used for medical reasons. There was no difference between the mean T-scores of the FZ abusers and those of the non-FZ abusers on the boredom-susceptibility scale. Nor was there a significant difference between the mean T-scores of the groups on the verbal aggression scale – again in contrast with the results from the study of juvenile delinquents (Study I, Table 3). There were no differences between the FZ abusers and non-FZ abusers on mean standard scores from the MNT, mean T-score scales from the EPQ-I, SSS-V, nor KSP.

## **Study III, and Letter to the Editor**

We selected some cases from the FZ abusers in the group of forensic psychiatric offenders admitted to an FPE in 1998, who had been convicted of murder or robbery, in order to illuminate some legal issues concerning the position of FZ in the health-care system.

The case studies showed that intoxication with FZ may be related to hostile behaviour and brutality: the abusers experienced an inflated sense of strength and became cold-blooded. Their crimes were extremely violent, and the perpetrators lacked both empathy and anticipatory anxiety, which contrasts with their customary behaviour based on their normal psychological characteristics. Their normal

psychological characteristics showed great uneasiness and reduced social ability, with a constant fear of doing something wrong. The media have openly discussed these cases, one of them in particular (see Study III, Case 1; and Dåderman et al., 2003). This participant showed several clear signs of psychopathic traits during the FPE, and because his crimes were extremely brutal, he has been studied in detail by Dåderman et al. (2003). This case (Case 1) was interesting, because another FZ abuser (Case 4, Study III) signed an “S” around the victim’s eye (eye gouging is an unusual type of assault). Case 1, which was also described in Study III (Dåderman et al., 2003), and who had not shown any sign of psychosis without FZ (he was an university student), murdered three victims. He became extremely violent, confused, and brutal under the influence of FZ. For example, after killing his first victim, he used the full force of his body weight on a broom handle to drive the eye of the victim into the brain. The bodies of the other victims were also brutally destroyed, and the male victim had an “S” signed around his eye. This case of an FZ abuser stimulated us to examine possible psychopathic traits in all FZ abusers (see Study IV). This case also provides an example of how Swedish law may work, and how important it may be for legal consequences if the police do not ascertain convincingly whether a perpetrator is intoxicated with FZ at the time of crime, in a case of a manipulative perpetrator (see also the *Discussion*).

Some incorrect information in Study III has been restified in a Letter to the Editor, and this letter is, thus, included in this thesis.

## **Study IV**

### *Substance use disorders in the pooled sample of offenders*

Fifty percent of the participants had alcohol use disorder, and 42% were cannabis or marijuana abusers. FZ, amphetamines and/or cocaine, and opiate (heroin) were abused by 34%, 32%, and 17% of participants, respectively. A measure of versatility of these five main types of substance use disorder in the participants was calculated, ranging from 0 (no use of the main five types) to 5 (five types of different substance use disorder) (see Study IV, Figure 2). The most frequent pattern of substance use disorder included only one type of the disorder. Four out of the 34 participants with only one type of substance use disorder were FZ abusers, and 21, 7 and 2 participants abused alcohol, cannabis, and amphetamines and/or cocaine, respectively, indicating that the majority of the FZ abusers were polysubstance abusers. None of the heroin abusers abused only heroin; every heroin abuser used at least two substances.

### *Results from the logistic regression analysis*

A stepwise logistic regression analysis was performed with FZ abuse as the dependent variable, and the four facets and group membership as independent variables (see Study IV, Table 4). Only one of the four facets, Facet 4 (Antisocial), was significantly correlated with FZ abuse according to the Wald criterion; 54% of the FZ abusers and 79% of the non-FZ abusers were correctly classified by Facet 4. The odds for a participant with a score above the threshold (a T-score of 61) being an FZ abuser were

four times greater than they were for a participant below the threshold, odds ratio = 4.30, 95% C.I. 1.86-9.94. This high odds ratio (4.3) shows a large change in the likelihood of being an FZ abuser on the basis of one unit change in the score on Facet 4. The group to which a participant belonged (the juvenile delinquent group or the forensic psychiatric group) did not enter the logistic regression equation.

The results suggest that abuse of FZ is more common in offenders who score highly on Facet 4.

#### *Relationship between each PCL-R item and FZ abuse, and validation of the findings*

The 20 PCL-R items and FZ abuse were analyzed using Student's *t*-test, and by a discriminant analysis following the stepwise logistic regression. Student's *t*-test showed that the mean scores for eight items were significantly higher in FZ abusers than they were in non-FZ abusers (see Study IV, Table 5). The same items contributed significantly in a discriminant analysis and in an initial logistic regression.

Only one of the items (Item 20, Criminal versatility) was significantly related to FZ abuse according to the Wald criterion,  $z = 13.49$ ,  $p < .00045$ , odds ratio = 3.72, 95% C.I. 1.85 - 7.50. The contributions of all of the other items were significant at a level above .10 after Item 20 had been entered.

The results suggest that FZ abuse has a high association with Item 20.

## **GENERAL DISCUSSION**

### **Summary of aims and main findings**

The main aims of this thesis have been:

- to determine the prevalence of substance use disorders, principally FZ abuse, in two populations of young men convicted of serious violent crimes
- to describe their backgrounds and type of offences
- to examine whether FZ abuse was reflected in the forensic psychiatric diagnoses of these participants
- to discover why they abuse just FZ (and not another substance)
- to discover whether the FZ abusers' behaviour changed when they were intoxicated with FZ and
- to examine how the abusers obtain FZ.

We wanted also to test whether scores measuring aggressiveness and sensation seeking, and scores on anxiety-related scales, were higher in FZ abusers than in non-FZ abusers. An additional aim was to study whether FZ abuse is associated with the typical characteristics of psychopathy. We hoped that the results would illuminate some legal issues and the special position of FZ on the Swedish legal and illegal market for drugs, in the light of its neuropsychopharmacological properties. These properties are markedly different from those of other potent benzodiazepines, especially when FZ is administered in a form that is different than the intended forms, and when the dosage differs from therapeutic doses.

The main results of the studies included in the present thesis can be summarized as follows:

- The prevalence of FZ abuse was high (40.4% in the juvenile delinquent sample and 30% in the forensic psychiatric sample) (Studies I and II). The most frequently abused substances were alcohol and cannabis or marijuana. FZ ranked third among abused substances in the pooled sample (Study IV), followed by amphetamines and/or cocaine, and opiates (heroin).
- The reasons reported for FZ abuse were similar in the two groups of FZ abusers (Studies I and II). There were two main reasons for FZ abuse. The main reason was to obtain an increased feeling of power and self-esteem, a feeling that everything is possible, which resulted in the FZ abusers change of perception of reality. The secondary reason, reported also by the majority of abusers, was to reduce the level of anxiety.
- The FZ abusers' behaviour changed due to intoxication with FZ. The reported side effects in both samples were as follows: anterograde amnesia, depersonalisation (heightened self-esteem, a feeling of power and strength, a "cold-blooded" personality), and aggressive reactions resulting in brutality (Studies I, II and III). In the juvenile group, the FZ abusers reported a reduction of anxiety (which was regarded by the abusers as a positive effect of FZ, because FZ reduced fear and insecurity, stimulated the belief that everything was possible), and it changed the abuser's perception of reality (similar to a state of psychosis) (Study I). Additional side effects reported by some participants in the forensic psychiatric group were enhanced anxiety, insomnia, excitation, nightmares, suspicion and irritability (Study II). Study III illustrates the above-mentioned side effects in five selected cases of FZ abusers.
- Juvenile delinquent FZ abusers reported that the experience of FZ intoxication when combined with alcohol differed from that of intoxication with other benzodiazepines, also when these were combined with alcohol. Other benzodiazepines combined with alcohol resulted in physical side effects (such as breathing difficulties and palpitations), which were considered as "dangerous". In contrast, FZ gave side effects that can be described as "mental" side effects (such as anterograde amnesia), and this property was considered as "desirable".
- The juvenile delinquent FZ abusers obtained FZ on an illegal drugs market, by stealing from pharmacies, from retired men and women (often their relatives), by stealing from other drug addicts, or from a supplier at parties (frequently available) (Study I); while the forensic psychiatric FZ abusers obtained the drug from general practitioners (Studies II and III).
- There were some associations between the participants' background characteristics and FZ abuse. In the juvenile delinquent sample, FZ abuse was significantly associated with the frequency of previous treatment occasions in a juvenile correctional institution, having experienced a childhood psychological/psychiatric contact, and living in a metropolitan housing area (Study I and the *Main Findings and Comments*). In the forensic psychiatric sample FZ abuse was associated with having previously undergone an FPE (Study II).
- FZ abuse was associated with past and present weapons offences and narcotics-related offences in the juvenile delinquent sample (Study I and the *Main*

*Findings and Comments*), and it was associated with the present sentences of robbery, weapons offences, narcotics-related offences and theft in the forensic psychiatric sample (Study II). The association between FZ abuse and robbery remained significant in the pooled sample of the participants (Study IV).

- FZ abuse was not frequently reflected in the psychiatric diagnosis received by the forensic psychiatric participants; only 4 out of the 18 FZ abusers received a diagnosis related to FZ abuse (Studies II and III).
- Mean raw scores on the KSP VA and SSS-V BS scales were higher in the juvenile delinquent FZ abusers than in non-FZ abusers (Study I). There were no significant differences between FZ abusers and non-FZ abusers in the forensic psychiatric group (Study II). Mean T-scores on the personality scales deviated in general from normative values (Studies I and II).
- FZ abuse was more common in offenders who scored highly on Facet 4 (Antisocial), and FZ abuse was associated with Item 20 (Criminal versatility). FZ abusers, however, were not characterised by the classic characteristics of psychopathy, such as lack of empathy, as seen in the fact that they did not score highly on Facet 2 (Affective). This is an important result, because it shows that FZ abuse is associated with such characteristics as poor behavioural control, early behavioural problems, juvenile delinquency, revocation of conditional release, and criminal versatility. These characteristics are associated more frequently with antisocial personality disorder, and are not typical psychopathic traits. This result may be helpful in the planning and management of treatment programmes for young offenders.

### **Comparison of the results with other findings**

The *Discussion* sections of the studies included discuss specific results, and the *Comments* included in this thesis present some alternative conclusions for each study. The results are, in general, novel and cannot be compared with other published studies. Exceptions are the results concerning the side effects of FZ, which agree with results concerning side effects reported by general practitioners (cf. Figures 1-4), and the results concerning polysubstance abuse, which are typical for the population of young offenders with mental disorders such as conduct disorder, ADHD, and personality disorders (e.g., Compton, Conway, Stinson, Colliver, & Grant, 2005; Rösler et al., 2004). Recent searching (14 October 2005) on a scientific data-base ([www.scirus.com](http://www.scirus.com)) has confirmed the novelty of the results presented here.

Those results of my work that can be compared with other published findings are discussed in this section.

#### *The extent of FZ abuse and an association with specific types of crime*

The prevalence of FZ abuse was high: 40.4% in the juvenile delinquent sample (Study I) and 30% in the forensic psychiatric sample (Study II). FZ abuse is a relatively “new” phenomenon, much newer than the abuse of many other substances (such as alcohol, cannabis and opiates), and it is therefore not surprising that previous research

in this respect in the juvenile delinquent and forensic psychiatric populations of male offenders is sparse.

Holmberg et al. (2002) reported findings from a project that is mentioned in the *Introduction*, which comprised 583 offenders undergoing a minor FPE (see Appendix 1 for a definition) and 416 offenders on remand, all of them being assessed during 2001. In the total sample of offenders, 36% used some type of benzodiazepine compound, and 121 participants were intoxicated with benzodiazepines while committing crimes; 64% of these 121 participants were intoxicated with FZ when committing the crime. Rohypnol was the most common compound among the benzodiazepines used; 40% of those who were intoxicated with benzodiazepines during the crime were intoxicated with Rohypnol. FZ was the most common benzodiazepine used by those who were intoxicated with benzodiazepines during the crime; 80% of those who were intoxicated by benzodiazepines during the crime in participants from the remand centres, and 39% of those who were intoxicated by benzodiazepines during the crime and who underwent their minor FPE, were intoxicated with FZ (and not another benzodiazepine). The use of benzodiazepines was significantly more frequent among younger (16-25 years) offenders than among older offenders. Interestingly, drug abuse is one of the most commonly reported mental health-related side-effects of FZ in the WHO's side-effects database (see the *Introduction*, Figure 3), and it is more commonly reported for FZ than for diazepam (Figure 4), and the high values of FZ abuse among offenders should not be an unexpected phenomenon.

Studies II and V concern young offenders (see the *Methods*). The studies showed that FZ abuse is significantly associated with robbery. This finding should be particularly interesting, 49% of all offenders who during 2004 had been accused of crimes of robbery in Sweden (Standar, 2005) were young people (aged 15-20 years of old).

Holmberg et al. (2002) summarised the findings from the project mentioned above, and pointed out that 29% of offenders who were charged with robbery (including robbery with violence) and who were subjected to a minor FPE were intoxicated with benzodiazepines during the alleged robbery, and they point out that the proportion of alleged offenders who were under the influence of benzodiazepines was significantly higher than proportions of offenders of other types of crimes (except for aggravated assault, see below).

The study by Holmberg et al. (2002) also showed that 20% of those charged with aggravated assault were intoxicated with benzodiazepines. This proportion was significantly higher than the proportion of offenders who were intoxicated with benzodiazepines and committed other crimes (except for the crime of robbery, which has already been mentioned above). Our studies (Study I and II) did not show a significant difference between those who commit violent crimes (except for the crime of robbery, see discussion above and Study II and IV). There are several explanations possible for this lack of such findings. One possible explanation is that we used different methods from those used by Holmberg et al. They considered the proportions of those who were (or were not) *intoxicated with all benzodiazepines* (including two "newer" benzodiazepine-like compounds, zopiclon and zolpidem,) during the *present* crime, while Studies I and II consider the proportions of those who were (or were not

*FZ abusers*), and this variable was then used in the statistical analysis in order to examine an association between FZ abuse and a particular type of crime.

Another possible explanation is a difference in the definitions of the variables used. In Study I (Table 2, row 1), a “violent offence” was defined as any conviction (up to the date of the study, including the “present” violent crime offence) for any kind of violent crime. This definition was independent of that of “serious violent offences”, such as murder, manslaughter, or serious cases of assault, which are presented separately in row 3. A “violent offence” was defined in Study II (Table 2) as an index offence, that is, a confirmed conviction for a crime, which led to the FPE. Another possible explanation lies in the fact that we did not account for all violent acts (i.e., even those for which the offenders had not been convicted). The following statement by a 20-year-old youngster from Stockholm, who had been using Rohypnol (and other drugs) may illustrate the present situation among young offenders: “Everyone I know who has done extreme things involving weapons, or who has really mistreated someone badly, has been under the influence of drugs. When you’ve taken drugs there are no barriers holding you back.” (Wierup, 2004).

The difference in definitions used (“intoxicated with a benzodiazepine during the crime” used by Holmberg et al. and “being an FZ abuser” used by us) makes the comparison of the findings somewhat difficult, but the majority of those who were intoxicated by benzodiazepines during the crime in Holmberg et al.’s (2002) study were FZ users, and those who used FZ generally fulfil the diagnostic criteria for FZ abuse according to DSM-IV, used in the studies described in this thesis. A questionnaire that I had constructed was used by Holmberg et al. (Holmberg et al., 2002, Appendix 1). This questionnaire was similar to the one used in Study II (see Appendix 1). In addition, all but three of the participants in Studies I and II, who were defined as “FZ abusers” were intoxicated with FZ during the crimes discussed.

FZ abusers while intoxicated are a high-risk group for committing serious crimes (Anglin et al., 1997; Dobbin, 1997; Elmgren, 1998; Hermansson, 1998; van der Laan, 1988; Rickert & Wiemann, 1998; Teo et al., 1979; and Studies I, II and III); for deviant driving behaviour (Druid et al., 2001); and for deaths by intoxication (Druid & Holmgren, 1997; Drummer, Syrjanen, & Cordner, 1993). It is sometimes difficult to grasp the severity of crimes committed by FZ abusers and non-FZ abusers when only studying and analysing the nature and frequency of the different crimes committed [Table 2 (Study I) or Table 1 (Study II)]. Behavioural changes when intoxicated were therefore clinically studied and described in detail in Study III. The FZ abusers claimed during qualitative interviews (all data not yet reported) that they would not have committed the crimes that they committed if they had not had access to FZ. (One may consider that they declared this in order to receive a milder sanction, but I was only a researcher and my judgement of their crimes or motivations would not have any legal status; they knew that the interviews were confidential and that I did not discuss their crimes with the staff.) These abusers claimed that the nature and the “severity” of their violent behaviour when intoxicated with FZ differed from the nature and severity of violent behaviour when intoxicated with, for example, alcohol or other drugs. This concerns, for example, the type and severity of injuries to their victims’ bodies.

Most FZ abusers committed the crimes under the influence of FZ or FZ together with alcohol. They may well have been under the influence of other drugs that were

probably already disappearing from the body, while the level of FZ was increasing rapidly, following recent intake. The serious nature of the actions, such as killing a brother or friend, is far removed from the actions associated with the normal personality of a person described as shy and anxious, a person who does not show aggression and, furthermore, has held positive feelings for the victim. It is true that alcohol intoxication in itself could explain a reduction of judgement and of impulse control, but the subsequent acts (such as biting the victim in the face, sticking a knife or broom handle into the eye, or a screwdriver into the body) are incomprehensible and bizarre. We conclude that the acts were carried out in a condition of psychological aberration under the influence of FZ and in some cases, under the combined influence of FZ and alcohol or other substances, but it is not possible to separate the extent to which the different substances influenced the condition of psychological aberration.

*The reasons reported for FZ abuse and the consideration that some side effects of FZ when combined with alcohol are “desirable” and other side effects are “dangerous”*

Several studies have shown that FZ is abused throughout the world, and that FZ is the drug of choice among some populations of opiate abusers (for a review see Woods & Winger, 1997). It is generally believed that opiate abusers use FZ to enhance the effects of low-quality heroin, while cocaine and amphetamine abusers use FZ as a remedy for the depression that follows a stimulant “high”, to allay withdrawal symptoms and to gain a state of oblivion (DEA, 1996; Woods & Winger, 1997). It is important to note that the FZ abusers in our studies did not use FZ in order to potentate or prolong the sedative effects of heroin or methadone, nor did they use it in order to attenuate the withdrawal effects of stimulants such as cocaine (as suggested by Woods & Winger, 1997). Gibert-Rahola, Maldonado, Mico, Leonseguí, and Saavedra (2002) have tested the hypothesis that benzodiazepine modifies the opioid withdrawal syndrome in mice. They induced morphine withdrawal syndrome by injecting naloxone, and then examined the effects of FZ and diazepam on the withdrawal symptoms experienced by the mice. All the signs of morphine withdrawal syndrome (such as jumps, paw tremor, teeth chattering) were antagonised by FZ and diazepam. Interestingly, “wet-dog-shake” signs were strongly increased by FZ, which may indicate that FZ is used by opiate abusers for reasons other than that of modifying withdrawal syndrome.

It is clear that the proportion of physical side effects reported by general practitioners for FZ is lower than that of diazepam (see the *Introduction*, Figures 1 and 2), and it is not surprising that juvenile delinquent FZ abusers reported (Study I) that they “liked” FZ better than other benzodiazepines, because FZ, when used together with alcohol, induced less other “dangerous” physical side effects (such as breathing difficulties and palpitations) than other benzodiazepines. No reports have been published that confirm a qualitative difference between FZ and other benzodiazepines concerning physical side effects, but Mattila and Larni (1980) cite a study of Tarnow et al. who showed that: “the decrease in peripheral resistance was 15% with flunitrazepam; in contrast diazepam did not decrease the peripheral resistance” (p. 358). Patients who receive extradural analgesia or general analgesia do experience differences (Mikkelsen, Hoel, Bryne, & Krohn, 1980). One month after injection

15.6% in the diazepam group, 8.5% in the flunitrazepam group and 9.3% in the saline group had pain or tenderness in the arm used for injection.

The affinities of the different benzodiazepines for their binding sites (peripheral and central) differ (Tallman, 1981). Braestrup, Albrechtsen, and Squires (1977) found, for example, that specific high-affinity binding sites for diazepam are present not only in the brain but also in several peripheral tissues, including the kidney. It is thus possible that different binding sites for different benzodiazepines differ in their properties of action, especially when combined with alcohol, and this issue may for this reason be relevant in a discussion of possible qualitative subjective differences of adverse physical side effects.

Evans, Funderburk, and Griffiths (1990) suggested that the lack of unpleasant side effects, which should logically include all physical side effects, gives a poor prognosis for freeing oneself from substance abuse. Furthermore, Bond, Seijas, Dawling, and Lader (1994) showed that FZ when taken nasally causes only three out of 13 possible physical symptoms – dizziness, physical tiredness and loss of concentration. As mentioned in the *Introduction*, Farré et al. (1996) studied equivalent doses of FZ (2 mg) and triazolam (0.50 mg). Both FZ and triazolam impaired performance in a test measuring a simple reaction time and digit symbol substitution test, but only FZ impaired the balance time (for the definitions see *Introduction*). The participants differed in their feelings of “physical” side effects. FZ gave significantly higher scores than placebo on the feeling of “high”, any effect, good effect, bad effect, liking, drowsiness, drunken, passivity and concentration, and significantly lower scores on activity and performance, while triazolam caused a significant increase in the scores on any effect and drowsiness.

Study I reported that FZ is considered more “practical” in the youngsters’ criminal activity. It is still possible, for example, to drive a car while intoxicated with FZ. It is difficult to discuss whether there are qualitative differences between FZ and other benzodiazepines concerning the ability to drive a car, but Mattila and Larni (1980) recommend refraining from driving a car or operating a machine for at least 24 hour after an intravenous administration of FZ, due to impairment in the co-ordination between eye and hand. It is possible that just FZ (and not other benzodiazepines) is regarded as “practical” by the present juvenile delinquents, because they are polysubstance abusers, whose abuse pattern includes alcohol abuse. Pycha et al. (1993) have shown that FZ is effective in the treatment of alcohol withdrawal delirium.

Bramness, Skurtveit, and Morland (2002) studied a population of suspected intoxicated drivers in Norway. This population included 10,759 cases containing only alcohol, and 818 cases containing only one benzodiazepine. The concentrations of benzodiazepines in the blood were well above therapeutic levels. Oxazepam and alprazolam were found more often in female drivers than in male drivers. Younger drivers had diazepam in their blood significantly more often than older drivers, and those who were older had more often oxazepam. Drivers who were involved in accidents had clonazepam in the blood more often than those not involved in accidents. These findings show clear differences in the pattern of benzodiazepine abuse among these drivers. Among those drivers who were intoxicated with benzodiazepines, 19% were considered to be “not impaired” by a physician using a standard clinical test for drunkenness, and there was no significant difference in this

respect between the different benzodiazepines studied. Those who were considered as “impaired” had significantly higher blood levels of diazepam ( $n = 411$ ), oxazepam ( $n = 73$ ), and flunitrazepam ( $n = 211$ ) than an average driver intoxicated with benzodiazepines in this sample. Bramness et al. conclude that the only characteristic that determines impairment is the concentration of benzodiazepines in the blood.

Anterograde amnesia is a well-known side effect of all benzodiazepines, but this effect seems to be more pronounced for FZ than it is for other benzodiazepines and the newer benzodiazepine-like compounds (see Figure 3 and references mentioned in the *Introduction*; for a review see, e.g., Kortilla & Linnoila, 1976). The members of the juvenile delinquent group considered this side effect as a positive side effect, because these offenders did not remember their acts, something that was highly practical in conjunction with police inquiries. The offenders undergoing an FPE, in contrast, considered anterograde amnesia as an adverse side effect. This difference of opinion concerning the value of anterograde amnesia may be considered in the context of the background characteristics (age and education) of the two samples of offenders (Table 5). It is possible that the negative experiences of the older offenders concerning this form of side effect have made their values more insightful. This issue has already been pointed out in Study II: “They found this effect of FZ very inadequate and awkward in many situations” (p. 34). FZ abusers described many violent situations during in-depth interviews (crimes for which they had not been caught and, therefore, not convicted; such crimes had not been reported) in which they found themselves confused and having “black-outs”. It happened that they found themselves in an emergency unit at a hospital without knowing why they were there (Study III).

The main reason for abusing just FZ, rather than any other substance, is to obtain an increased feeling of power and self-esteem, a feeling that everything is possible. Several clinicians and social workers have described abusers’ feelings when intoxicated with FZ in the same terms. Nilsson (1998), for example, cited a polysubstance user’s statement of how an abuser felt when he took FZ: “Nothing really matters, you know. You become invincible. Your brain sorts of blocks everything out.” Juvenile delinquents in our study reported 2-6 mg of FZ as the most “desirable” dose range, and they reported that the effects of a particular dose varies from person to person and from one occasion to another.

Another FZ abuser who murdered three persons (one of the five cases described in Study III, for whom more detailed studies are described in Dåderman et al. 2003) described his feelings related to different doses of FZ. The offender could take a dose that, according to him, was tailored for a special purpose. For example, when he took 4-6 mg of FZ he “felt a frozen feeling in his stomach, and at the same time a pleasant feeling”, which he described as if his brain was asleep (Dåderman et al., 2003, p. 24), but when he took other dosages it felt different (data not reported). Analysis of some street names of Rohypnol may to some extent “validate” this claim. The Australian street name of FZ is “Rambo”. Dobbin (1997) states that this street name expresses the effect it has on a person, who receives the courage required to commit crimes by consuming FZ. One of the street names of FZ in the United States is “roofies”. This name was given to the drug by Mexican building workers who, after consuming FZ, were able to work on roofs at high levels without the fear of falling.

Professor Björn Beerman, spokesman at the Swedish Medical Products Agency, has also pointed out this special effect of FZ. He said that FZ is a perfect drug for a person who intends to commit a crime since “this compound gives a sort of supereffect, and mixing it with spirits just drives you crazy” (Brising, 2002).

The majority of FZ abusers also reported that FZ reduced their level of anxiety, and this state was considered by juvenile delinquents as highly desirable (Study I), particularly in situations of punishment, and to avoid having to face up to social norms. Haggård-Grann, Hallqvist, Långström, and Möller (2005) have recently reported results from their study of 133 violent offenders (offenders who had undergone an FPE and offenders from a Swedish National Prison Evaluation Unit in a Swedish prison in Kumla, outside Örebro). They showed that regularly used therapeutic doses of benzodiazepines are not associated with an increased risk of violence, while there is a clearly increased risk that those who use benzodiazepines at doses higher than therapeutic will carry out violent acts. The FZ abusers who participated in the studies described in the present thesis used doses higher than normal (for a definition of “therapeutic dosage” see the *Introduction*, Note No. 5).

Inciardi and Surratt (1998) reported that the abuse of FZ is common among street-children in Brazil. Many street-children in Brazil see their use of FZ and other drugs as an escape – a means to dull their hunger and facilitate acts of prostitution and crime. There are between seven and eight million street-children, aged from 5 to 18 in Brazil, but it is not known how many of these children abuse FZ. As mentioned in the *Introduction*, FZ is abused by street-children in the Egyptian city Alexandria (Salem & Abd El-Latif, 2002). Rohypnol is the only benzodiazepine whose use is described by Salem and Abd El-Latif, and they point out that compounds with hallucinogenic effects are especially dangerous because the hallucinations they produce “lead to improper spatial orientation resulting in violent behaviour, crimes and traffic accidents” (pp. 7-8). All the street children behaved aggressively and violently, by damaging the surrounding environment, fighting with other people, showing aggression towards other people’s possessions, or by starting fires. It is difficult to rule out “escape from reality” as the reason for FZ abuse in our results. The quotations presented in Figure 5, and the process of using the grounded theory analysis, give an impression that the FZ abusers in the juvenile delinquent group used FZ in a similar way, to change their perception of reality. There are, naturally, many differences in the family situations and in other social factors between Swedish juvenile delinquents and Brazilian street-children, and Egyptian street-children. There is hopefully no need for anyone to feel hunger in Sweden, and no participants were compelled to prostitute themselves in our sample. The desire to avoid feeling guilt for their crimes (cf. Figure 5: “When I stabbed him it felt like putting a knife into butter”) may be the common factor between these youngsters.

There is another group of FZ abusers who desire to change their perception of reality and who may be compared here with the male juvenile delinquents, and that is female opiate abusers who also abuse FZ. Many female opiate abusers are compelled to prostitute themselves, and they take FZ in order to escape the shame and fear associated with prostitution. Nilsson (1989) cited a statement of one such prostitute: “Heroin doesn’t help when you’re ashamed and scared, you still know what’s going on. You have to take Rohypnol instead to deaden your feelings.” Recent findings from

a larger group of offenders on remand and being screened for an FPE (Holmberg et al., 2002) confirm the present findings to some extent; about 40% of benzodiazepine users combined several substances with benzodiazepines because “they had wanted mood elevation (escape from boredom, increased intoxication, a kick, and enhanced effect)” (p. 17); 64% of the benzodiazepine users in this study were FZ abusers.

Another pattern of the abuse of FZ has been revealed in reports of date rape (Anglin et al., 1997; Rickert & Wiemann, 1998), in which the perpetrators slipped FZ into women’s drinks in order to induce sexual relations, because of the ability of FZ to affect will-power. The victim knows that something is happening but is unable to stop it. It is claimed that FZ reduces the victim’s judgement, inhibitions, or physical ability to resist sexual advances. FZ induces amnesia, which often results in the victim not being able to remember what has happened. None of the present FZ abusers used FZ in order to affect the will-power of a potential rape victim.

Calhoun, Wesson, Galloway, and Smith (1996) and Schwartz and Weaver (1998) are among researchers who have reported that students at high schools and colleges in the U.S. use FZ to enhance disinhibition when they “party”. Adolescents and young adults at rave dances use the drug to experience a euphoric “high”, similar to that induced by alcohol intoxication. Many of the juvenile delinquent participants in the studies reported here used FZ while they attended rave parties. It is possible that these participants differed from the other party-goers in respect of their personality pattern.

#### *Are diagnoses of substance use disorders included in FPEs?*

Alcohol abuse should be taken into account when FZ-related behaviour is studied. In our groups, 61% of juvenile delinquents and 40% of forensic psychiatric participants were alcohol abusers (*Methods*, Table 5), according to DSM-IV criteria, although only 25% of the forensic psychiatric participants received a DSM-IV diagnosis of alcohol use disorder as a result of the FPE (Wennberg & Dåderman, 2000). We considered (Wennberg & Dåderman, 2000) whether participants had received serious criticism for alcohol abuse, which is one of diagnostic criteria of alcohol abuse according to DSM-IV (American Psychiatric Association, 1994; see also the *Introduction*, the subsection *Definition of FZ abuse as an example of substance-related disorders (DSM-IV)*). The forensic psychiatric participants had received on average more criticism for alcohol abuse than a male control group taken from a Swedish cohort; nearly 70% of forensic psychiatric participants had been seriously criticised for their alcohol habits, compared to 25% of the control group. The forensic psychiatric participants had developed a greater tolerance to alcohol than a control group; more than 50% reported an increased alcohol tolerance, compared to about 20% of the control group (Wennberg & Dåderman, 2000). These results indicate that alcohol abuse in the group of forensic psychiatric participants is higher (see above, 40%) than the level that appears from official information (25%) based on their FPE. Thus, traditional diagnoses of substance use disorders (such as alcohol) are not always stated in the results of an FPE.

It should also be pointed out that diagnoses of other “unusual” substances that may theoretically be abused by the violent offender population (for a recent discussion, which concerns a change pattern of drug abuse in both violent offenders and their

victims, see Thiblin & Petersson, 2005) did not result in psychiatric diagnoses (see the *Methods*) either, but there are only a few cases who abused, for example, anabolic steroids (data not reported). Among juvenile delinquents, five out of the 47 participants abused anabolic steroids (see Study I, Table 3), and only one of them was also an FZ abuser. If abuse of this substance were more common, it would be necessary to discuss the possible effects of contemporary or previous abuse of anabolic steroids on the side effects of FZ intoxication. The use of anabolic steroids may result in brutality (Thiblin, Kristiansson, & Rais, 1997), and rats that receive anabolic steroids prior to amphetamines may respond with amphetamine-induced aggression (Steensland, Hallberg, Kindlundh, Falke, & Nyberg, 2005).

Thus, it is not surprising that diagnoses related to FZ abuse, which is a relatively new form of substance abuse, were not frequently stated in the results of an FPE. Only four out of the 18 forensic psychiatric FZ abusers received a diagnosis related to FZ abuse (Studies II and III). Table 1 (Study II, p. 31) suggests that the abuse of FZ has often been described in forensic files (often by social workers), and that forensic psychiatrists may not always have been aware how important the diagnosis of FZ abuse is. Even a traditional substance abuse, alcohol, was not assessed in all cases. We suggest that psychiatrists pay more attention to the offenders' abuse patterns. (Other types of abuse stated at an FPE have not been compared with the diagnoses given for participants in the present project.)

FZ has received increased attention from law enforcement agencies in a number of countries in recent years (see the *Introduction* sections in Studies I – V for examples). Abuse of FZ is now a well-recognised worldwide problem, and it should be a topic of discussion among forensic psychiatrists. The complex, and psychiatrically significant, relationships between diagnosis, “traces” of FZ abuse in forensic files, actual convictions, and previous forensic psychiatric assessments are clearly seen in Table 1 and Table 2 (Study II). The fact that such traces exist indicates that it is often another member of the forensic team (usually a social worker) who describes the FZ abuse, and not the member of the team who is responsible for the DSM-IV diagnoses. It should be noted that other, more “established” types of abuse, such as alcohol abuse and amphetamine abuse, are more readily recognised. Even though the abuse of FZ was a world-wide problem during the year in which Study II was carried out (1997-1998), forensic psychiatric teams did not consider FZ abuse, and thus did not recognise this disorder.

All participants were asked during the interviews to describe situations in which they do something dangerous under the influence of alcohol or drugs (Wennberg & Dåderman, 1999; 2000). The most frequent answer was that they often drive a car while drunk. Despite the fact that the participants often drive when influenced by alcohol or drugs (Wennberg & Dåderman, 1999; 2000), this behaviour was not reflected in the convictions of the participants' convictions prior to the current FPE. Only three out of the 60 participants had such a conviction. Druid et al. (2001) found that one out of four intoxicated drivers who were either caught in routine police controls or stopped because of deviant driving behaviour was intoxicated with FZ.

It is also remarkable that several forensic psychiatric FZ abusers did not have any psychiatric diagnosis of sleep disorder or anxiety disorder (see *Methods*), while notes in the forensic files show legal medication against such disorders (see Study II, Table

1). This may be due to the fact that the participants generally lacked several “obvious” diagnoses (such as ADHD, reading disorder, anxiety disorders) in their FPE. About 40% of the forensic psychiatric sample (Dåderman, Lidberg, & Lindgren, 1999; Dåderman & Lidberg, 2005; Selenius et al., 2005) suffered from reading and writing disabilities, according to DSM-IV, but only a few subjects had received such a diagnosis during the FPE. This is remarkable, since such diagnoses are expected in a sample like this (e.g., Rösler et al., 2004).

There were no diagnoses according to DSM-IV given in the institutional files of the juvenile delinquents. The only clear diagnosis was that they all suffered from conduct disorder, because they had been placed in care in institutions that take care of juvenile delinquents with this kind of problem. Juvenile delinquents suffer from dyslexia (Dåderman et al., 2005) and from dysfunctions associated with this disorder, such as poor verbal memory (Selenius, Dåderman, & Hellström, 2005), ADHD and other neuropsychiatric dysfunctions (Anckarsäter, Nilsson, Saury, Rastam, & Gillberg, 2005; Anckarsäter, Ståhlberg et al., 2005; Dalteg & Levander, 1998; Siponmaa, Kristiansson, Jonson, Nydén, & Gillberg, 2002; Ståhlberg, Söderström, Rastam, & Gillberg, 2004; Ståhlberg, Anckarsäter, Gillberg, & Rastam, 2005; Söderström & Nilsson, 2003; Söderström, Nilsson, Sjödin, Carlstedt, & Forsman, 2005; Söderström, Sjödin, Carlstedt, & Forsman, 2004), various mental disorders and associated dysfunctions of the brain (Adler, Frisk, & Lidberg, 1995; Alm, 1996; Mattson, Schalling, Olweus, Löw, & Svensson, 1980;), and there is an overrepresentation of juveniles with psychopathic and other deviant personality traits (Dåderman, 1999; Dåderman et al., 2001; Dåderman & Kristiansson, 2003, 2004).

The lack of focus on FZ-related substance use disorders by those conducting FPEs during 1997-1998 is surprising, because FZ abuse among offenders undergoing an FPE and who were convicted of homicide had already been discussed in 1993 by a fellow of The Committee for Forensic Psychiatry, Social and Medical Legal Questions at the Swedish National Board of Health and Welfare (Elmgren, 1998). We hope that the publication of the studies mentioned in the *Introduction*, which are included in a book entitled *Lugnande läkemedel som oroar* [Sedative substances that make us anxious] (Holmberg et al., 2002), has raised awareness of the need for stating FZ abuse-related diagnoses, and other diagnoses of substance use disorders.

### *Personality traits in FZ abusers*

We postulated that FZ abusers show the same personality patterns as alcohol abusers, since alcohol and sedatives (of which FZ is an example) are substances that “share similar” characteristics (DSM-IV, p. 175). Benzodiazepines, alcohol, barbiturates, and neurosteroids are example of what are known as “positive allosteric modulators of the central GABA<sub>A</sub> receptors”, and these substances increase aggressive behaviour in several species, often to excessive levels (Miczek, Fish, & De Bold, 2003). It was interesting for this reason to examine whether the participants had high scores on aggression-related personality scales. Many participants in the group of juvenile delinquents comprised “Type 2 alcoholics” (Cloninger’s classification; see e.g., Cloninger, Bohman, & Sigvardsson, 1981). Type 2 alcoholics begin drinking at an early age (before 25 years), they have a high frequency of alcoholism and depression

in first degree relatives, a high frequency of substance use disorders and social complications, they display sensation-seeking behaviour, extraversion, and their levels of platelet MAO activity are low (von Knorring, Bohman, von Knorring, & Orelund, 1985). Alcohol abusers often abuse benzodiazepines, including FZ (Busto, Sellers, Sisson, & Segal, 1982). Our unexpected result was that there are few differences in personality scale scores (KSP VA and SSS-V BS) between FZ abusers and non-FZ abusers in the juvenile delinquent group (Study I), and no personality trait differences in the forensic psychiatric group (Study II).

Tables 2-4 in the *Introduction* show that there are some differences between alcohol abusers and non-abusers measured by the EPQ, SSS and KSP scales. King et al. (1995) showed that alcohol abusers score higher in the EPQ N and P scales. EPQ scales are often associated with different substance abuse patterns, where higher scores in psychoticism and neuroticism characterize substance abusers (see Table 2). We have, however, not found such elevated scores in the groups of FZ abusers we studied. People with different substance use disorders tend to score higher on the total SSS scale (Table 3), while those with alcohol use disorders score higher than non-abusers on the SSS ES and Dis scales. Marra et al. (1998) showed that Type 2 alcoholics score higher on the SSS TAS scale. FZ abusers, however, scored higher than non-abusers in the SSS-V BS scale. Alcohol-abusers with higher scores on the BS scale reported less satisfaction with an addiction treatment programme (Duaux et al. 1998), while alcohol abusers scored higher than stimulant abusers, opiate abusers and polydrug abusers on this scale (O'Conner et al., 1995). Scores on the KSP VA scale were higher in the juvenile delinquent group of FZ abusers studied here, but only a few previous studies (Table 4) have recorded a similar result in the drug-abusing population. For example, Type 2 male alcoholics were characterized by higher scores on the KSP VA scale (L. von Knorring, A. L. von Knorring et al., 1987).

Figures 1 and 2 (Study I) and Figure 1 (Study II), and results presented by Dåderman (1999), clearly show that many personality scale scores in the participants differ from published normal scores. It is generally the case that it is more difficult to show subgroup differences in groups with deviant characteristics, and this may be one reason that we did not find more personality differences between FZ abusers and non-FZ abusers. Another explanation is that specific personality traits that predispose to FZ abuse do not exist (except for the traits of boredom susceptibility and verbal aggression in juvenile delinquents). It is possible that the state-behavioural characteristics (related to sensation seeking, psychoticism, impulsiveness, and hostility; and expressed in crimes such as robbery, weapons offences, and theft) observed in FZ abusers when intoxicated with FZ are induced by FZ *per se*, sometimes combined with other substances, and that the “normal” personality traits of the abuser (i.e., their “everyday” personality, without the influence of the drug) do not play a role.

## **Thesis limitations**

### *Generalization of the results*

The main limitation of this thesis is the population studied, and the fact that the results cannot be generalized to other populations. The selection of the participants in both

groups of offenders was carefully carried out (see *Methods* and Dåderman & Kristiansson, 2003, p. 203 for discussions concerning how representative the two groups were). For example, all potential juvenile delinquents in the four institutions and all offenders referred for an FPE at the Department of Forensic Psychiatry in Stockholm who satisfied the inclusion criteria were asked to participate. We suggest that the results may be generalized, and are valid at least for male offenders from the population of serious juvenile delinquents in Swedish youth correctional institutions and nonpsychotic Swedish-speaking, offenders under 35 years of age who undergo an FPE, and who were on remand. Most of the participants had some type of mental disorder (see the *Methods*), as defined by DSM-IV (American Psychiatric Association, 1994), and it is thus possible that the generalization may be extended to male offenders with other types of mental disorders from other populations, but this generalization should be made with caution.

#### *Focus on only one substance use disorder*

One shortcoming of the work presented in this thesis may be its focus on FZ abuse only. Other substance use disorders are presented in the published articles, which to some extent overcomes this shortcoming (see Study I, Table 3, p. 94; Study II, Table 1, p. 31; Study III, Table 1, p. 244; Study IV, Table 1). Furthermore, a correlational analysis was conducted in the most recent study (Study IV) in order to investigate whether other main substance disorder types are associated with the different facets of PCL-R (see Study IV, Table 3). The main five types of substance use disorder in the pooled sample of participants (DSM-IV) were alcohol, cannabis and/or marijuana, FZ, amphetamine and/or cocaine, and opiate abuse, and a measure of versatility of abuse was calculated for these five types. The logistic regression carried out, however, (Study IV) focused only on FZ abuse.

#### *Lack of person-oriented methods*

One may consider that the work presented in this thesis did not use person-oriented methods (for one example of such methods used on the present sample of juvenile delinquents, see Dåderman & Kristiansson, 2004), and that it focuses solely on variable-oriented statistical analyses (such as the calculation of correlation coefficients and reliability coefficients, Student *t*-test, analysis of variance, logistic regression, discriminate analysis). Person-oriented methods (such as cluster analysis) are more sophisticated and may give more information regarding particular homogenous subgroups of participants within the sample (Bergman, 1988; von Eye, 1990). This additional information may be subsequently available to aid in the treatment.

#### *Definition of FZ abuse in the studies included*

Some participants included in the studies are labelled “FZ abusers”. The majority of these participants lacked a psychiatric diagnosis of FZ abuse (or FZ dependence). This means that the forensic psychiatrist (for the offenders referred for a forensic psychiatric evaluation) or the clinical psychiatrist (for the juvenile delinquents) had not

diagnosed FZ abuse according to DSM-IV. This problem, and to some extent the problem of the absence of various other diagnoses (e.g., neuropsychiatric disorders, such as dyslexia and ADHD, or anxiety-related and depression-related diagnoses), has already been discussed (e.g., Dåderman & Kristiansson, 2005; Dåderman & Lidberg, 2005; Trygg et al., 2001). We introduced the term “acute intoxication with FZ” (Study I), due to the fact that the juvenile delinquents in this study were very young (on average, 17 years), and they had not yet received a diagnosis according to DSM-IV from a psychiatrist. Most of the institutional psychiatrists described only the participants’ ordinary mental status in the institutional files (for example, if a participant was psychotic or not), without presenting other, commonly found disorder diagnoses among juvenile delinquents (e.g., ADHD, conduct disorder, disorder of reading expression, or substance use disorders).

All but three of the FZ abusers included in the studies described in this thesis fulfil one or more of the DSM-IV criteria for substance (FZ) abuse, independently of whether they had a current psychiatric diagnosis of abuse of or dependence on FZ. The three exceptions (Study II) were subjects who had suddenly decided to stop the abuse. This group stated that they previously abused FZ (at which time they had fulfilled the DSM-IV criteria for the abuse of FZ), but this had not occurred within a 12-month period before the time of our assessments, and they did not continue the abuse prior to the assessments.

To sum up, we assessed all FZ abusers in the studies according to the DSM-IV criteria. In some cases, our diagnoses overlapped with psychiatric diagnoses recorded in the participants’ files. In almost all cases, however, we found “traces” (i.e., verbal descriptions in the files, but no diagnoses) of FZ abuse in certain files, and these were the participants who were designated as “FZ abusers” (see, for an example Study II, Table 2).

### *Qualitative analysis*

A grounded theory analysis (Glaser, 1978), using constant comparison procedures (Glaser & Strauss, 1967), has been applied to answer why FZ abusers abuse just FZ (and not another substance) (Study I). We have presented only the main findings of this part of the study and we have not described the process of finding the appropriate answer to the study question (such as, for example, the coding scheme, see Figure 5 and detailed citations) for the following reason. My co-author and I presented the findings at several seminars and meetings during the period 1997-1999, and discussed the findings with several experts in the field of pharmacology and addiction. The findings were sometimes severely criticised, and were considered as extremely controversial at the time. Thus, we decided to examine an additional population until the credibility (or the trustworthiness – a term used to describe the validity of a qualitative study) of the findings could be established beyond doubt, using fully adequate evidence. We believed that similar relationships between phenomena would emerge from data derived from other populations of FZ abusers, and that new categories (see Figure 5) might emerge from new data. A manuscript based on the extended sample is being prepared, while a preliminary diagram of the major

categories, their relationships and supporting quotations, based on qualitative interviews with 19 FZ abusers, is shown in Figure 5 in the *Methods*).

In this qualitative study (see Figure 5 and Study I), I successfully reached almost all potential responders from the population studied; only three out of 63 potential participants refused to participate (I do not know whether those who refused were FZ abusers or non-FZ abusers). This high participation rate enabled us to study the phenomenon of FZ abuse in a well-defined population. The breadth of the qualitative inquiry was enhanced by studying the participants' files, and by studying their personalities and mental health. The number and the nature of the data collection points within the examination enhanced its depth. Interviews carried out at early stages of the research lasted longer than those carried out later, when questions become more focused. This is consistent with the procedures used in examining the grounded theory. I had begun the interviews among the juvenile delinquent FZ abusers who were detained in the high-security department at the Sundby School. Their experiences with FZ use were rich. The description of findings included the use of participants' terminology, identified by quotations, that I hope will facilitate the reader's understanding of important ideas. One limitation is that only one person has carried out the data sampling and the analysis. It should be pointed out that it is not unusual for an individual researcher to sample, analyse, and report qualitative data (see e.g., Cohen, 1999; Newman, 1993; Reynolds, 1996; Roberts, 1999).

## **Implications of the findings**

### *Clinical implications*

Some conclusions from the studies included in the present thesis may have clinical implications. The most important of them are listed below, and briefly discussed.

The first clinical implication that should be recognized is that the prevalence of FZ abuse is high in the population of mentally disordered male offenders. This means that clinicians from forensic psychiatry and those who take care of forensic psychiatric patients and juvenile delinquents should be constantly aware of the possibility of FZ abuse, and, naturally, the abuse of other substances (such as other benzodiazepines and newer benzodiazepine-like compounds, and all possible substances that may have an association with serious crimes). The abuse of legal and illegal substances should always be accurately diagnosed. Offenders with this type of abuse must not, for example, be given the opportunity to have leave from a forensic psychiatric clinic, without a careful supervision. There is a risk in this case that they will become influenced by FZ or similar compounds, and become impulsive, brutal and psychotic as a consequence (cf. Elmgren, 1998). Unfortunately, FZ is readily available on the illegal market. All members of society have the right to protection against offenders who, while intoxicated with potent drugs (such as FZ), may act as Dr Jekyll and Mr. Hyde.

The second implication that should be recognized concerns the association between FZ abuse and Facet 4 (Antisocial) of the PCL-R. The probability that an offender is an FZ abuser is more than four times greater if the offender attains high scores on Facet 4. Clinicians who have the opportunity to assess offenders (or potential

offenders) should focus their attention on the attainment of high scores on Facet 4. High scores on Facet 4 are characterised by the following criteria: poor behavioural control, early behavioural problems, juvenile delinquency, revocation of conditional release, and criminal versatility (Hare, 2003). The last criterion (Criminal versatility) should receive particular attention, because this criterion was the only significant predictor in a logistic regression analysis for being an FZ abuser. It is possible that an “educational programme” for general practitioners in the criteria of Facet 4 will help to protect society from the negative consequences of FZ abuse.

We should keep in mind that the offenders who score high on Facet 4 have a four-fold higher risk of being an FZ abuser (Study IV). This fact should be considered in the risk assessment and prevention process (see the discussion included in Study IV).

### *Implications for “crime scene” investigations*

Knowing some of the characteristics of a “typical” FZ abuser may be useful for “crime scene” investigators. How should the police reason when faced with an offender who does not remember anything, appears confused, and has a bloody knife in his hands?

The findings from the studies described in the present thesis allow us to sketch an outline of a juvenile delinquent offender: he is a young sensation-seeking person with elevated scores on the SSS-V BS scale. He cannot stand watching a movie that he has seen before, he gets bored seeing the same old faces, he cannot enjoy a movie or play in which he can predict what will happen in advance, looking at someone’s home movies, videos, or travel slides bores him tremendously, he considers people for whom he can predict almost everything they will say or do to be boring, he prefers friends who are excitingly unpredictable, he gets very restless if he is forced to stay at home for any length of time, the worst social sin he knows is that of being a bore, he likes people who are sharp and witty even if they do sometimes insult others, and he has no patience with dull or boring persons (these statements are cited from Zuckerman, 1994, Appendix A). In addition, this juvenile delinquent has elevated scores on the KSP VA scale. It means that he uses “strong language” when his anger is aroused, he cannot help getting into arguments when people disagree with him, he is apt to tell anyone who annoys him exactly what he thinks of him, he says nasty things when he gets mad, and he yells back when people yell at him (these statements have been cited from Schalling, 1986).

Other typical background characteristics of a juvenile delinquent FZ abuser are the following: to have had contact with childhood psychological or psychiatric institutions, to have been previously cared for at a juvenile correctional institution (probably at least three times), to be living in a metropolitan area, to have one parent with an immigrant background, and previous sentences for weapons offences and for narcotics offences.

The profile given above will be useful for crime scene investigations where there is no apparent motive for the crime. The police should always seek after empty packages of tablets in order to secure evidence of abuse.

The present findings may also be useful in investigations concerning a somewhat older offender whose memory of the crime is impaired. He may be a potential FZ abuser (or an abuser of other potent benzodiazepine compound or other

benzodiazepine-like compounds – intoxication with FZ should be regarded as an example of more general abuse of similar compounds). The only characteristic that distinguishes him from a non-FZ abuser is that he has previously been subjected to an FPE, and has been convicted of robbery, weapons offences, narcotics-related offences or theft.

### *Legal issues*

Doctors in general practice write about 90% of the benzodiazepine prescriptions in Sweden. Mellergarg (1993) reported that only 30% of these prescriptions are related to psychiatric diagnoses.

The perpetrator of a serious crime in Sweden cannot be sentenced to prison if it is shown that the crime was committed under the influence of a “serious mental disorder”, and that a causal relation exists between the crime and the disorder (Socialstyrelsen, 1996; see Appendix 1 for more details). Intoxication with FZ or with other similar compounds is associated with behaviour that is displayed under what is most likely a state of serious mental disorder, but this state disappears when the influence of FZ wears off. The perpetrator often has no memory of his crime and sometimes denies committing it, despite obvious evidence (such as being in the victim’s apartment with a blood-stained knife in his hand). Such considerations may make the decision for a particular perpetrator (serious mental disorder or not) more complicated. There is praxis in Sweden, that a self-inflicted substance intoxication causing, for example, a psychotic state or temporary dissociation states, is not regarded as a serious mental disorder. Thus, a substance-induced state of confusion or psychosis or other serious mental disorder (according to DSM-IV), does not normally mean that the offender is subjected to forensic psychiatric care (except for rare cases of so called pathological intoxication, when a small amount of a substance unexpectedly causes a psychotic-like state), unless FPE finds that a primary psychosis or other serious mental disorder was the main reason for the actual crime and that the adverse effects of the intoxication with a substance was of secondary importance.

Case 1 in Study III (see also Dåderman et al., 2003) shows that the abuse of FZ raises an important legal issue – can people who experience psychosis or a state of “dissociative syndrome” while under the influence of FZ be diagnosed as suffering from a serious mental disorder. The case also illustrates that the interpretation of the concept “serious mental disorder” and the application of the law may be inconsistent. Bukhanovsky et al. (1999) studied ten cases of perpetrators of eye gouges, as it is known that eye gouging has been used as a method of terrorism and as a punishment to enforce social norms. It is interesting that only four of the cases studied were classified as psychotic at the time of the eye assault, and one of the four cases became free of psychotic symptoms after a short period of treatment. Moreover, three of the four psychotic cases were classified as polysubstance abusers (intoxication with FZ or with other similar substance was, however, not assessed).

The forensic psychiatric team that studied the perpetrator described in Case 1 of Study III (see also Dåderman et al., 2003) decided that the crime had not been committed under the influence of a serious mental disorder, and that there were no signs of a serious mental disorder during the FPE. This conclusion was confirmed by

other sources, for example, the forensic and other official files, and by discussions with persons who knew the perpetrator well. The police investigation of a further crime of murder was not yet complete, so the team requested a reassessment of this case. The reassessment decided that the offender had suffered from a serious mental disorder at the time of the crime. The reassessment concluded that the offender suffered from a severe form of antisocial personality disorder with features of narcissism and borderline, together with a “dissociative syndrome” (the forensic doctor choose this psychodynamic term rather than using the term in DSM-IV: “dissociative disorder”). The use of this dubious terminology, together with media opinion and an intense debate between leading forensic psychiatrists, psychiatrists, and philosophers (see Study III and Dåderman et al., 2003, for references), led to the court sentencing the offender to forensic psychiatric treatment. It is also possible that the expectations of society in general (“No normal person can perform such crimes”) influenced the court. This case raises the following questions: What treatment is suitable for this subject? How long must he remain in forensic psychiatric treatment to remedy his syndrome?

One indirect implication of the results reported here concerns the risk assessments and therapy programmes used for juvenile delinquents. Correctional institutions in Sweden are operated by the state, and the therapy that is most widely used is environmental therapy. The need for risk prediction that is based on the assessment of a multi-professional team in collaboration with the staff (Kristiansson, 2002), and the best way of determining appropriate mental health care in the population of juvenile delinquents, have been discussed (e.g., Anckarsäter et al., 2005). Environmental therapy dominates the treatment of juvenile delinquents in Sweden in 2005; 11 of the 35 institutions use cognitive behavioural therapy. The abuse of different substances is a dynamic risk factor, in contrast to sociological risk factors (such as sex, parents backgrounds etc.), which are static risk factors, and the abuse may be prevented by applying evidence-based treatment programmes, and by societal actions (such as to declare “dangerous” compounds as illegal). Appropriate assessment procedures concerning all mental disorders (such as dyslexia, ADHD, and different types of substance-related use disorders) as well as psychopathic traits, following guidelines outlined in the DSM-IV (American Psychiatric Association, 1994), should be used. Without appropriate diagnoses, a particular therapy is meaningless. It is not surprising that the received treatment in these institutions was ineffective; we found a significant association between being an FZ abuser and the frequency of previous treatment occasions in a juvenile correctional institution (see Study I and the *Main Findings and Comments*). Research into the effectiveness of different treatment programmes for juvenile delinquents should be more intensive.

Another indirect implication of the results reported here concerns the assessment methods used in an FPE. Kempe (2003) and Tilus (2005) studied forensic psychological methods used for the assessment of male offenders undergoing an FPE, and Trygg (2000) studied the methods used in the present sample of male offenders undergoing a major FPE. The results showed that the use of projective tests for assessing personality was more frequent than the use of psychometric tests. These findings were discussed by Trygg et al. (2001), Hallman (2001), Kristiansson (2001), Crona et al. (2001), Mattlar et al. (2001), and Wiklund et al. (2002). There is no

evidence to suggest that the proportion of the use of different methods has changed in recent years, in spite of the fact that the Swedish National Board of Health and Welfare points out that forensic psychological assessment should be based on methods of good empirical quality (Socialstyrelsen, 1996).

### *Theoretical implications*

We have shown that there are significant personality trait differences in the sample of 47 juvenile delinquents with respect to boredom susceptibility and verbal aggression. We have presented a psycho-neuropharmaco-biological theory (Study I, Figure 3, p. 95) of these differences, based both on our findings and on findings from previous research into impulsive violent behaviour. This theory explains paradoxical rage reactions from intoxication with FZ as a result of a disinhibition phenomenon in the serotonergic mechanism and a result of personality traits assumed to arise from the biological basis of personality. The theory that Lidberg and I have proposed is a psycho-neuropharmaco-biological theory concerning FZ-induced impulsiveness (see Study III), resulting in violent acts in specific persons who possess possible psychopathic traits with elevated levels of high verbal aggression and high boredom susceptibility. We arrived at this theory partly as a result of studying research into a metabolite of serotonin found in the CSF, 5-hydroxyindoleacetic acid (5-HIAA). We suggest (see Study I and Figure 5) that the increased feeling of power and self-esteem produced by FZ may result in FZ-induced impulsiveness, and that both phenomena may interact with each other. It is commonly assumed that impulsiveness is characterised by a person's inability to wait for a stimulus before acting (e.g., Ainslie, 1975; Eysenck & Eysenck, 1977; Twain, 1957).

Impulsiveness is a characteristic of a number of deviant behaviours (such as violent acts and suicide), and it is included as a diagnostic criterion in some disorders (such as kleptomania and bulimia). Impulsiveness has been linked to a reduction in the level of serotonergic transmission (for reviews see Åsberg, Schalling, Träskman-Bendz, & Wägner, 1987; Coccaro, 1989; Kruesi et al., 1990; Orelund, 1993, 2004; Orelund & Shaskan, 1983). Previous research has shown that suicides in which a violent method is used (such as hanging, shooting or self-stabbing) are associated with low concentrations of 5-HIAA in the CSF (for a review, see Åsberg, 1994). It is assumed that all benzodiazepines affect the GABA receptor system (e.g., Tallman, 1981; and for review DEA, 1996; World Health Organization, 1996) and in this way may indirectly lower serotonin activity in the brain (Lidberg and I have discussed this issue with other researchers at several meetings, see Dåderman & Lidberg, 1999). Animal studies have shown that benzodiazepines decrease serotonin function (Laurent, Mangold, Humbel, & Haefely, 1983; Saner & Pletscher, 1979; Trulson Preussler, & Howell, 1982), and in this way indirectly increase impulsiveness (Dietch, & Jennings, 1988; Gantner, & Taylor, 1988; Soubrié, 1975; Bizot & Thiébot, 1996). It is interesting that both diazepam and FZ decrease the synthesis of serotonin in the hippocampus in the rat brain (Nishikawa & Scatton, 1986).

It should be pointed out that both samples of participants had higher values of impulsiveness than normative samples (see Studies I and II; Dåderman, 1999; Dåderman et al., 2001), measured on different scales, but the FZ abusers did not differ

from non-FZ abusers in this respect. Impulsiveness may be expressed by several forms of behaviour that include impulsiveness aspects, such as novelty seeking, poor behavioural control, and disinhibition (for a review see Dawe, Gullo, & Loxton 2004). The result is not surprising, because substance abusers are generally impulsive (see e.g., the *Introduction*, Tables 2-4 for findings concerning the measures used in the studies described in the present thesis). It must, however, be kept in mind that the present participants are polysubstance abusers, and it is possible that other substance abuse than FZ abuse differentiates significantly between the impulsiveness levels of abusers and non-abusers.

It may be useful to consider arousal theories when discussing FZ abuse. The arousal theory proposed by Robbins (1997) presented together with Eysenck's model, and the biological "vulnerability model" presented in the *Introduction* are particularly useful. FZ, like other benzodiazepines, facilitates the effect of GABA at the GABA<sub>A</sub> receptors, and in this way inhibits large regions of the brain. However, FZ differs from some other benzodiazepines in that it is a potent compound with a rapid rate of onset of action, a long duration of action (for definitions see World Health Organization, 1996), and high values for the pharmacodynamic properties of receptor affinity and efficacy (see the *Introduction*). It should also be noted that FZ has a number of active metabolites that affect clinical behaviour long after the drug has been administered, and that the effects of the metabolites may, especially during the prolonged repeated treatment that is not unusual in FZ abusers, equal or exceed those of the parent compound. The metabolites of some benzodiazepines (e.g., diazepam) have a higher affinity for the GABA<sub>A</sub> receptor complex than the parent compound (Greenblatt, Sahder, Weinberger, Alleh, & McLaughlin, 1978). Some pharmacological effects of FZ (for a review see DEA, 1996; World Health Organization, 1996) may differ in vulnerable subjects who have a pattern of personality traits that may predispose them to react in a special way. This difference in reaction is compatible with the biological vulnerability model (see the *Introduction*), with lower activity of serotonin in the brain of these users, and with other genetic differences. This special reaction may occur when a vulnerable person is exposed to environmental stressors, such as stressful situations, disease, or intoxication with various substances, including FZ.

Dawe et al. (2004) have recently proposed a theory, the implications of which are that impulsiveness is higher in the substance-abusing population. They point out that impulsiveness is a heterogeneous concept, and many measures of impulsiveness are associated with each other. Recent studies, however, indicate that impulsiveness has two dimensions, labelled "reward sensitivity" ("heightened sensitivity to the reinforcing effects of substances accompanied by a greater propensity to develop conditioned responses" p. 1398), and "rash impulsiveness" ("response disinhibition, or the inability to inhibit prepotent approach tendencies" p. 1398). The studies described in this thesis may exemplify different forms of impulsiveness, which may be expressed in impulsive behaviour (such as nonplanned violent behaviour) while intoxicated with FZ, and not in any traditional measures of personality traits. It is evident that the participants continue their abuse of FZ (except for the three participants who had experienced hostility as an undesirable and unexpected side effect). FZ abusers are significantly more impulsive than normative samples, but they are not more impulsive than non-FZ abusers from the population studied. Poor behavioural control, which is

an example of impulsiveness, is a component of Facet 4 of PCL-R, and this component is associated with four-fold increase in the risk of being an FZ abuser. We suggest that FZ abusers are a special group of substance abusers that need a treatment programme that has been specially designed for them.

### *Some specific neuropsychopharmacological issues*

Neurotransmitter receptor systems have been the focus of intensive pharmacological research for more than 20 years, but the actions of specific drugs at different receptor systems are only now becoming clear (Korpi et al. 2002).<sup>16</sup>

Many FZ abusers also abuse other substances, and it is possible that the numbers of various receptors change in FZ abusers' brains due to their polysubstance abuse. The numbers of some receptors present vary over a day by as much as 50% (Rosenzweig et al., 1999). The daily rhythms of a subject change due to long-term amphetamine abuse or combined amphetamine and alcohol abuse, independently of any FZ abuse that may be present, and thus the number of receptors in a particular receptor system probably also changes. Other chemical and physiological changes in the brain occur due to a poor glucose supply caused by the poor and irregular eating habits of such abusers. The World Health Organization (1996)<sup>17</sup> has stated that: "All else being equal, benzodiazepine absorption can be affected by several factors including food, concurrent therapy and position of the body. Thus a slowed and decreased absorption occurs in the reclining position, in the presence of food in the stomach or when a benzodiazepine is administered together with an aluminium containing antacid." (p. 7). The World Health Organization suggests that there are large intra-individual differences in the pharmacokinetic characteristics of a particular benzodiazepine, especially when other forms of administration are used; and the WHO states, for example, that the effects of an intramuscular form of administration, "may be delayed and unpredictable" and "intravenous administration, bypassing absorption, results in a more rapid onset of activity, mainly determined by the time it takes for the drug to diffuse across the blood brain barrier." (p. 8).

The most common adverse effect of FZ arising from its psychopharmacological properties is complete or partial amnesia. This effect is particularly marked if FZ is taken with alcohol. Sometimes, FZ abusers found themselves in hospital or a police station, and could not remember why they were there, since their episodic memory (that is, their memory for personal experiences) was impaired (Study II). The amnesic effects produced by FZ are desirable in a clinical setting: when FZ is used as a presurgical medication, for example, the amnesic effects can diminish the unpleasant memories related to surgical procedure. However, amnesic effects are not always

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<sup>16</sup> This should be kept in mind, because FZ has been approved in Sweden since 1980, without sufficient knowledge concerning the neurotransmitter receptor system involved. The only studies that were available in 1980 for the Department of Drugs at the National Board of Health and Welfare (Socialstyrelsens läkemedelsavdelningen) were 28 studies summarized by Professor Björn-Erik Roos. The studies concerned mainly intravenous anaesthesia with FZ. I received this information from the Swedish Medical Products Agency when I enquired about the studies on which the approval of FZ as a legal substance in Sweden was based (Gertrud Heed, Läkemedelsverket [The Swedish Medical Products Agency], personal communication, 6 February 2004).

<sup>17</sup> Ulf Rydberg, Department of Clinical Neuroscience, Clinical Alcohol and Drug Addiction Research, Karolinska Institutet, was one of these professors in pharmacology who contributed to this report.

desirable in offenders. The present thesis has shown that memory loss allows FZ abusers to forget experiences of previous violent acts, consequently influencing their behaviour. The drug can be used to avoid a sense of guilt for violent offences, and to provide a useful loss of episodic memory when faced with inquiries. Most adult FZ abusers found this effect unpleasant, in contrast to most juvenile FZ abusers, who found it practical. This difference in attitude to such “black-outs” may be a result of the difference in average age (about ten years).

The differences between the clinical effects of FZ and other benzodiazepines with respect to several psychological functions may have important implications for criminal behaviour. However, it is not known whether the specific clinical properties of FZ depend on the drug effect *per se*, or on individual differences in genetics, on functional and/or structural differences in the brain, or on individual differences in the metabolism of the drug. The dosage is also important, because the differences in effect depend on the patients’ age, sex, weight, any disease from which they suffer, and tolerance to the drug, where this has developed (see also “sök läkemedel”, 2005). It is clear that the sedative effect is dose-related, but it is also clear that some behavioural effects of FZ are not dose-related (for a review see DEA, 1996).

The work presented in this thesis has shown that behaviour alters while under the influence of FZ. It has shown that male juvenile delinquents and young male forensic psychiatric patients convicted of serious crimes have a pattern of personality traits that indicates psychiatric or psychological vulnerability. Previous research on personality traits has shown that many such deviant traits are linked to dysfunction of the monoamine system in the brain, in particular a low level of serotonin. This indicates that vulnerable persons react with abnormal behaviour (such as aggression, a special form of sensation-seeking behaviour, or impulsiveness) in many situations (for example, in stressful situations). Some unique neuropsychopharmacological properties of FZ may trigger abnormal behaviour during intoxication with FZ, and these properties may interact with other factors in stressful situations, to produce lower activity of serotonin in the brain. This then enhances impulsive and inhibited behaviour.

The studies described in the present thesis suggest that FZ provides some FZ abusers with effective biological and unusual cognitive “protective” strategies against fundamental moral rules (such as that of not killing a brother, or not assaulting an already unconscious or inanimate body). Examples of these strategies have been provided through an analysis of the nature of violent crimes while intoxicated with FZ (Study III). It is not known which psychopharmacological properties of FZ, or which combination of such properties with temporary changes (e.g., environmental influences), lead to brutality. This suggestion must be considered carefully. Comparing the severity of violent crimes and their relationships with intoxication with different substances will need to be carefully considered.

### **The need for further research**

The World Health Organization has recently stated that: “the prevalence of anxiety and insomnia and the consumption of sedative hypnotics are growing, the elderly being the main group of consumers. The INCB notes with concern the frequent long-term use

(beyond one year and sometimes indefinitely) of psychotropic substances for treating psychological reactions to social pressure without diagnosis for a specific disorder. The abuse of these drugs and others such as benzodiazepines and other anxiolytics continues to be widespread in many countries and requires appropriate vigilance and countermeasures” (World Health Organization, 2005). Future research concerning benzodiazepines should, first and foremost, focus on collaboration between forensic psychiatry, forensic medicine, biological psychology and biological psychiatry, neuroscience, genetics and pharmacology.

Suggestions for future studies:

- The prevalence of the use and abuse of certain newer benzodiazepine-like compounds should be determined. This work should focus on compounds that may be associated with aggression and disinhibited and impulsive behaviour, which may result in brutality, and it should focus on the offender population of both males and females. Such a study should also include the use and abuse of anabolic steroids.
- It is important to determine why abusers of specific substances abuse just these (and not another substance). I believe that qualitative methods have a great advantage, because it is difficult today to receive the funding required to conduct large studies. Qualitative methods (such as the grounded theory analysis), which focus on only a few well-defined participants, should be used to a greater extent in areas in which previous research is lacking.
- It will be of a great value to design a study among a specific group of substance abusers, such as FZ abusers or abusers of the newer benzodiazepine-like compounds (see Table I). This study design may include questions concerning changes in behaviour while intoxicated.
- A more focused design, which also may include an analysis of the brutality of all violent acts, including violent acts for which an offender has not been convicted, should be of great interest. An analysis of forensic autopsies should be included in the project.
- It will be important to examine whether forensic psychiatrists diagnose specific forms of abuse, including the abuse of benzodiazepines. The work should cover psychiatric diagnoses in all departments of forensic psychiatry.
- Research into the effectiveness of different treatment programmes for juvenile delinquents should be intensified.
- High-resolution brain imaging of subjects intoxicated with substances that may lead to disinhibited and impulsive behaviour should be performed. It is important to know which regions of the brain are most affected by a specific substance. Little is known about the brain dysfunction of specific abusers.
- Ludford and Schara (1981) suggest: “Psychopharmacological experiments to explore which areas of the brain are responsible for which effects. Of special interest should be to relate benzodiazepine receptor occupancy to the reinforcing effects of the drug” (p. 93).
- The possible association between FZ and impulsiveness may be examined by designing animal studies that would confirm or deny the hypothesis that FZ lowers the activity of serotonin in the brain and that this is the mechanism by which FZ stimulates inhibition-free or impulsive behaviour.

- Comparative studies should examine long-acting and short-acting benzodiazepines and benzodiazepine-like compounds in different deviant populations, for example in those with personality disorders, including psychopathy. Are the pharmacokinetics of different benzodiazepines different due to specific personality traits?
- Environmental factors, such as the poor dietary habits of polysubstance abusers, should be examined, and the effect of such factors on the affinities of different benzodiazepines to sites on the GABA<sub>A</sub> receptor complex system.
- The prevalence of the use of potent benzodiazepines and benzodiazepine-like compounds and the occurrence of possible adverse effects of these compounds in the elderly should be determined.
- The reasons for the failure of governments and society to prevent the widespread availability of dangerous substances should be explored. Special attention must be paid to the protection of vulnerable members of society, such as adolescents and those suffering from a mentally disorder.

## Conclusions

FZ abuse is common in a nonpsychotic population of younger serious offenders, which is generally characterised by mental disorders, such as conduct disorder, dyslexia, ADHD and personality disorders, and by low self-esteem, deviant personality traits, psychopathic traits and lifestyle, and a high prevalence of mixed substance abuse. FZ abusers have described how FZ may induce disinhibition, impulsivity and anterograde amnesia, and temporary dissociation states. These offenders were involved in serious crimes while intoxicated with FZ, and most of them were recidivists.

A failure to diagnose the abuse of FZ creates an economic burden and a security risk for the community. FZ was often taken without proper medical supervision despite the fact that most of the forensic psychiatric FZ abusers had been prescribed FZ by their doctors. The abuse often occurred in combination with the abuse of alcohol, amphetamines, cannabis, or other benzodiazepines. This pattern of drug abuse, and its combination with serious crimes, poses a health risk to the abusers and a risk for the surrounding community. Juvenile delinquents stated that they desired to abuse FZ in order to increase the feeling of power and self-esteem, to reduce fear and insecurity, and to stimulate the belief that nothing is impossible. While intoxicated with FZ, they were able to achieve a generally calm, “anti-anxious”, and methodical state, which was desirable before committing crimes; they did not feel an empathy with the victims. (The studies described in the present thesis were not designed to show quantitative differences between different benzodiazepines.)

Young offenders should not be able to obtain FZ, because crimes of robbery, weapons offences, narcotics-related crimes, and other crimes (such as theft) are more prevalent in the FZ abusers than in non-FZ abusers. In addition, the probability that an offender is an FZ abuser is four times greater for those with high scores on Facet 4 (Antisocial) than it is for those who are low on this facet. There is, however, no correlation between Factor 1 from the PCL-R and FZ abuse, which may indicate that the drug *per se* may “induce” or “entice” bad classic psychopathic traits such as a lack of empathy, leading to temporary dissociation states (“Dr Jekyll and Mr Hyde”?)

The best way to reduce these risks is to take the legal decisions necessary to withdraw potent abused drugs such as FZ from the market, not only in Sweden, but also in other countries. Patients with sleep disorders and anxiety disorders can be treated just as well with other drugs, or with behavioural treatment programmes. Greydanus and Patel (2005) have recently described the drug situation in the U.S. and concluded: "Finally, perhaps most importantly, societal apathy about the problem of drug abuse needs to be replaced by a determination to improve and correct the current unfortunate and yet correctable situation in America" (p. 96).

The most important conclusion of the studies described in the present thesis is that one of the most potent benzodiazepines, which acts rapidly at the GABA<sub>A</sub> receptor complex system, is very frequently abused by young offenders in Sweden, and while intoxicated with FZ, their perception of reality may change, leading to lack of empathy during temporary dissociate states.

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## Legislation in Sweden concerning offenders with mental disorders

### *Legislation*

The present thesis concerns young offenders with a high prevalence of different forms of mental disorder, as specified by DSM-IV (American Psychiatric Association, 1994), including conduct disorder (predominantly in the juvenile delinquent participants), different forms of personality disorder, reading disorder, disorder of written expression, and different forms of substance use disorder (for details see *Methods*).

Legislation in Sweden concerning the assessment and treatment of offenders who have committed serious crimes has some characteristic features not found in other countries. Sweden has a legal concept, “serious mental disorder”. The current legislation was introduced in Sweden in 1992 (for details see Kullgren, Grann, & Holmberg, 1996). According to the Swedish penal code, the defendant may not be sentenced to prison if the crime was committed under the influence of a “serious mental disorder”. If a serious mental disorder is still present at the time of sentencing, the offender receives forensic psychiatric care. Serious mental disorder is judged to be present if a perpetrator suffers from a psychotic disorder (regardless of aetiology, and thus psychotic “states” can be classified as serious mental disorders), from rare cases of particularly serious depressive disorder with the risk of suicide, serious personality disorders (only in limited cases, which include “serious loss of impulse control or the presence of psychotic features”), serious dementia, serious mental retardation or a mental disorder with marked compulsive disorder. In these cases, the mentally ill perpetrator of a serious crime is sentenced to forensic psychiatric care, or, in rare cases, probation. A sentence to forensic psychiatric care is based on the results of a forensic psychiatric evaluation (FPE) (see below). Those who are sentenced to forensic psychiatric care are still considered “responsible” for their crime (i.e., “guilty”).

An FPE in Sweden is performed according to certain guidelines, and lasts for 2-4 weeks. The assessment must be completed within 4 weeks if the offender is on remand. If the offender is not on remand the FPE must be completed within six weeks.

### *Forensic psychiatric assessment and some legal issues*

There are four main forensic psychiatric departments in Sweden. The staff at two of them – Huddinge (which lies close to Stockholm) and Göteborg – are state-employed. These staff only assess the offenders, and do not treat them. Huddinge is the largest department, and carries out about 50-60% of all FPEs, while Göteborg carries out about 30%. The staff at the remaining two units (Malmö and Umeå) are employed within the health care system (hälso- och sjukvården), and both carry out FPEs and provide forensic psychiatric care.

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An FPE in Sweden is requested by the court. The aim of an FPE is to decide: (a) whether the offender suffered from a serious mental disorder at the time of the crime; (b) whether the offender suffers from a serious mental disorder at the time of the FPE; (c) whether there is a need for forensic psychiatric care and whether the preconditions for entrustment to forensic psychiatric care are present; and (d) to assess the risk of relapse into new crimes and consider whether forensic psychiatric care under a special court order is required. About 1% of all cases of serious crimes lead to the perpetrator being subjected to an FPE.

There are two types of FPE, “major” and “minor”. A minor assessment is performed in order to decide whether a major FPE is needed. A court can only request a major FPE if there is clear evidence that the person is guilty of a serious crime (one for which sanctions more serious than a fine are possible) or if the offender has confessed the crime of which he or she is accused. The majority of offenders who are referred for a major FPE are on remand, but there is also a possibility to be referred for this investigation without being on remand. (In the studies described in the present thesis, Studies II-IV, only forensic psychiatric offenders who were on remand have been included.)

An FPE results in a written report that includes extensive reports from a team comprising a psychologist, a forensic psychiatrist and a social worker, supplemented with a report from the nursing staff. The reports are based on observations from the nursing staff, repeated clinical interviews, assessment of social functioning with relatives, and an extensive forensic psychological assessment.

The Committee for Forensic Psychiatry, Social and Medical Legal Questions (Rättsliga rådet) at the Swedish National Board of Health and Welfare (Socialstyrelsen) re-assesses about 5% of all major FPE cases (while almost no minor FPEs are subjected to this re-assessment), and the court commissions an expert opinion in these cases. The committee in about half of these cases changes the decision reached during the FPE. A fellow of the committee prepares the opinion (for descriptions of such cases see Elmgren, 1998, 1999). This procedure is used for cases that are particularly difficult to assess.

During 1998, the year of the core data sampling for the forensic psychiatric sample (Studies II-IV), 1,841 offenders were referred for a minor FPE, and 609 to a major FPE; a total of 314 offenders were sentenced to forensic psychiatric care following a major FPE (Rättsmedicinalverket [The Swedish National Board of Forensic Medicine], 1999). More than 95% of those who underwent an FPE were found to have a psychiatric disorder; about half of them fulfilled the criteria for a serious mental disorder. Forensic psychiatric care was recommended in about 45% of cases, while probation or care by the social welfare system was recommended in 10%. The court nearly always follows the recommendations of the forensic psychiatric team.

### *Swedish national correctional institutions for juvenile delinquents*

Juvenile delinquents who are at least 15 years old may be referred for an FPE, and may therefore receive forensic psychiatric care in one of the special forensic psychiatric clinics. It is however, very rare, that juvenile delinquents are referred for an FPE. In the present sample of 55 juvenile delinquents, only two were also members of

the forensic psychiatric sample and a total of 11 participants have ever been referred for any form of FPE (i.e., minor or major FPE) (including a follow-up period; for details see *Methods* and Study IV).

In Sweden, children and adolescents less than 20 years of age who are convicted of crimes are often taken care of by the social welfare system, and, thus, only rarely imprisoned (Rättsnätet, 2005). A decision to place an offender into care in a state-administered correctional and observational institution for “young persons with problems”, called “a special approved home”, is not time-limited, and the lengths of stay vary between a few weeks and two years. The length of the commitment depends on the behaviour of the offender during the care. The Swedish Social Welfare Board reconsiders the detention after every 6-month period. Swedish law states that a juvenile delinquent who has been placed into institutional care because of his or her own criminality or substance abuse may remain in the institution up to the age of 21. Most juvenile delinquents in the SiS institutions have been placed there without their consent, because it was considered that they “are in danger of injuring themselves or of ruining their lives” (see “The National Board of Institutional Care”, 2005, see the *References*). During 1996, the year of the core data sampling for the juvenile delinquent sample (Study I), there were 35 such institutions, which took care of 575 juveniles (girls and boys) between 12 and 21 years of age. Fifteen of these institutions took care only of male juvenile delinquents, aged 15 to 21 years, who had “serious psychosocial problems, with elements of criminal behaviour and substance abuse”.

The aim of the treatment in an SiS institution is: “to help the young person concerned to achieve development and maturity and to equip him or her for a life without violence, drugs and crime” (the interested reader may find these citations and links to Internet-based information concerning SiS organization, its commission, clients, etc. at “The National Board of Institutional Care”, 2005). The Swedish treatment programmes for institutionalised juvenile delinquents in 1996 were based mainly on “environmental therapy”, which is, according to SiS (“miljöterapi”, 2005; Larsen, 1997), historically based on psychodynamic theory. An “environmental therapy” is “aimed at developing and maintaining a stable and developmental social structure” (“miljöterapi”, 2005), and SiS has stated that questions regarding social relationships have an exceptional importance for the treatment of juvenile delinquents.

The current legislation, the Care of Young Persons (Special Provisions) Act (see e.g., “closed institutional youth care”, 2005; Lidberg & Wiklund, 2004), allows the possibility also for serious offenders aged 15 to 18 (if the crime was committed between the ages of 15 and 18) to receive care in a special institution within the National Board of Institutional Care (Statens institutionsstyrelse, SiS) instead of prison. In these cases, the nature of the crime, and not the need for care, determines the length of sentence; it may vary from 14 days to 4 years. A court decides whether a particular juvenile delinquent is to receive care within the closed institutional youth care or whether he or she is to receive a prison sentence. The operation of the National Board of Institutional Care is regulated by “Lagen om verkställighet av sluten ungdomsvård” [“The Implementation of Closed Institutional Youth Care Act 1998:603”].

## Frågor rörande bruk av flunitrazepampreparat (FZ) <sup>1</sup>

## Appendix 2

1. Har du någon typ av missbruk?

OM JA: Specificera

2. Har det hänt någon gång att du använt Rohypnol eller andra tabletter som innehåller flunitrazepam (FZ)?

OM JA: Vilket eller vilka av dessa preparat? (FZ = Rohypnol, Flunitrazepam NM Pharma, Flupam, Fluscand)

3. Har det hänt någon gång att du misskött dina ordinarie uppgifter för att du var påverkad eller abstinent efter FZ?

OM JA: Hur ofta?

4. Har du kört bil när du varit ordentligt påverkad av FZ?

OM JA: Hur många gånger har det hänt?

5. Har det hänt att du blivit tagen av polisen på grund av FZ?

OM JA: Har det hänt flera gånger?

6. Har ditt bruk av FZ lett till problem med andra (till exempel familj, vänner)?

7. Har du råkat för slagsmål när du tagit FZ?

8. När använde du FZ första gången?

9. Hur fick du tag på det?

10. Hur får du tag på det nuförtiden?

OM LEGALT: Vad är anledningen till förskrivning?

11. Hur många tabletter tar du per dag?

12. Hur många tabletter tar du vanligtvis per gång?

13. På vilket sätt tar du det?

14. Händes det att du tar det samtidigt med alkohol och/eller andra droger eller läkemedel?

OM JA: Vilka?

OM JA: Vilken effekt vill du uppnå genom att blanda?

15. Har du varit påverkad av FZ vid det aktuella brottet?

16. Har du varit påverkad även av alkohol och/eller andra droger eller läkemedel (t ex andra bensodiazepiner) vid det aktuella brottet och/eller dagen före brottet?

Nr: .....

Ja Nej

Ja Nej

Jag föredrar följande FZ: .....

Jag brukar även följande FZ: .....

Ja Nej

Ibland Många gånger

(Ange årtal) .....

Läkare Illegalt

Läkare Illegalt Både och

Sömnproblem Ångest/Oro Osäkerhet

Smärtor Annat: .....

..... (ange styrkan per tablett: .....

..... (ange styrkan per tablett: .....

Tabletter Injicieras Inhaleras

Ja Nej

Alkohol Droger: .....

Ja Nej

Ja (alkohol) Ja (droger/läkemedel:

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**Questions concerning the use of flunitrazepam (FZ) <sup>1</sup>**

**Appendix 3**

1. Do you abuse any substances?

If yes, give details

2. Have you ever abused Rohypnol or other tablets that contain flunitrazepam (FZ)?

If yes, specify which of the substances (FZ = Rohypnol, Flunitrazepam NM Pharma, Flupam, Fluscand)

3. Have you ever failed to carry out properly your normal tasks because you were intoxicated with FZ or suffering withdrawal symptoms?

If yes, how often?

4. Have you ever driven while noticeably intoxicated with FZ?

If yes, how many times has this happened?

5. Have you ever been apprehended by the police due to FZ?

If yes, has this happened on several occasions?

6. Has your use of FZ caused problems between you and other people (such as family and friends)?

7. Have you ever got into a fight after taking FZ?

8. When was the first time you used FZ?

9. How did you get hold of it?

10. How do you currently get hold of it?

If by a legal manner: why is it prescribed for you?

11. How many tablets do you take a day?

12. How many tablets do you normally take at a time?

13. How do you take it?

14. Have you ever taken it together with alcohol and/or other drugs or medicines?

If yes, which others?

If yes, what were you trying to achieve by mixing FZ with other substances?

15. Were you intoxicated with FZ when committing the crime?

16. Were you intoxicated also with alcohol and/or other drugs or medicines (such as other benzodiazepines) when committing the crime and/or during the preceding day?

No: .....

Yes                      No

.....

Yes                      No

I prefer the following FZ form: .....

I also use the following FZ forms:.....

.....

Yes                      No

Occasionally      Frequently

Yes                      No

Occasionally      Frequently

Yes                      No

Occasionally      Frequently

Yes                      No

Occasionally      Frequently

(Give the year) .....

Doctor                      Illegally

Doctor                      Illegally                      Both

Sleep problems      Anxiety                      Uncertainty

Pain                      Other: .....

..... (give the tablet strength: .....

..... (give the tablet strength: .....

Tablets                      Injected                      Inhaled

Yes                      No

Alcohol                      Drugs: .....

.....

.....

.....

Yes                      No

Yes (alcohol)      Yes (drugs/medicines:.....

.....

.....

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